

Supplementary Material B

Characteristics of the included studies

Supplementary Table B1: Included studies (emboldened studies were significantly effective at post-treatment in pairwise meta-analyses)														
Study reference	Country	Study Design	Participants		Type (code for meta-analysis)	Demographic and Disease Factors			Primary target or Outcome	Fatigue Outcome (primary; secondary; emboldened outcomes were selected for the NMA)	Post- intervention time-point: (wks)	Attrition at post-treatment (%)	Final follow-up time-point: wks post- intervention	
			Exp. <i>n</i>	Ctrl. <i>n</i>		Exp.	Ctrl.	Exp.						
Exercise studies														
1. Ahmadi et al. 2013 (1) + ¹	IR	RCT	10	10	Treadmill training (aerobic)	Waitlist (TAU)	NR; 36.80 (9.17); 100%; EDSS: 2.40 (1.24); 5.6 (3.30) yrs.	NR; 36.70 (9.32); 100%; EDDS: 2.25 (1.25); 5 (3.05) yrs.	NR	FSS (NR)	8	0	0	NR
2. Ahmadi et al. 2013 (2) + ¹	IR	RCT	11	10	HATA Yoga (general)	Waitlist (TAU)	NR; 32.27 (8.68); 100%; EDSS: 2 (1.09); 4.72 (5.62) yrs.	NR; 36.70 (9.32); 100%; EDDS: 2.25 (1.25); 5 (3.05) yrs.	NR	FSS (NR)	8	0	0	NR
3. Alguacil Diego et al. 2012 ^ ²	ES	RCT	18	16	Whole body vibration (combined)	No-intervention (TAU)	NR; 43 (17); 52.; 94%; EDSS: 3.99 (0.80); NR.	NR; 44 (20); 47%; EDSS: 3.99 (0.80); NR.	NR	FSS (NR)	1	5%	12%	NR
4. Atri et al. 2012 # ³	IR	RCT	14	12	Aquatic exercise (general)	NR (TAU)	NR; 36.3 (7.81); 100%, EDSS: 2.4 (1.1); NR.	NR; 31.50 (7.96); 100%; EDSS: 2.8 (1.5); NR.	Fatigue	FSS (NR)	8	NR	NR	NR
5. Aydin et al. 2014 +x ⁴	TR	RCT	20	20	Hospital-based callisthenic exercise (combined)	Home-based callisthenic exercise (combined)	100%; 32.62 (3.15); 56%; EDSS =3.6 (1.3); 6.43 (2.78) yrs.	100 %; 33 (4.06); 55%; EDSS = 3.4 (2.1); 7.40 (3.43) yrs.	NR	FSS (NR)	12	20%	0	NR
6. Azimzadeh et al. 2012 ^ ⁵	IR	RCT	43	24	Tai Chi Chuan (general)	TAU	100%; NR; 100%; EDSS Range: 1-5.5; NR.	100%; NR; 100%; EDSS Range: 1-5.5; NR.	NR	Energy subscale of MSQoL-54 (NR)	12	65%	25%	NR

7. Bansi et al. 2012 + ⁶	CH	RCT	30	30	Water Ergometer (combined)	Land Ergometer (aerobic)	NR; 50 (44.6 to 55.1); 68%; EDSS: 4.6 (4.0 to 5.2); NR.	NR; 52 (46.7 to 56.3); 64.28%; EDSS: 4.7 (4.1 to 5.3); NR.	a) Interleukin, Tumour Necrosis Factor-Alpha b) brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF)	FSMC (S)	3	20%	6%	NR
8. Brichetto et al. 2013 *+ ⁷	IT	RCT	18	18	Wii® Balance Board (balance)	Balance rehabilitation (balance)	NR; 40.7 (11.5); 55%; EDSS 3.9 (1.6); 11.2 (6.4) yrs.	NR; 43.2 (10.6); 67%; EDSS: 4.3 (1.6); 12.3 (7.2) yrs.	Berg Balance Scale (BBS)	MFIS (S)	4	0	0	NR
9. Brichetto et al. 2015 + ⁸	IT	RCT	16	16	Personalised Balance Rehabilitation (balance)	Traditional Balance Rehabilitation (balance)	56.3%; 50.1 (13.5); 69%; EDSS: 3.7 (1.1); 9.5 (6.6) yrs.	62.5%; 51.0 (8.9); 75%; EDSS: 3.7 (1.4); 12 (6.2) yrs.	Berg Balance Scale (BBS)	MFIS (S)	4	0	0	NR
10. Briken et al. 2014 (1) + ⁹	DE	RCT	12	11	Rowing (aerobic)	Waitlist (TAU)	SP&PP 100%; 49.1 (8.5); 50%; EDSS: 4.7 (0.8); 14.1 (6.1) yrs.	SP&PP 100%; 50.4 (7.6); 60%; EDSS: 4.9 (0.9); 18.9 (9.8) yrs.	Aerobic fitness (VO2 and heart rate)	MFIS (S)	8-10	8%	9%	NR
11. Briken et al. 2014 (2) + ⁹	DE	RCT	12	11	Arm ergometer (aerobic)	Waitlist (TAU)	SP&PP 100%; 50.9 (9.2); 63.63%; EDSS: 5.2 (0.9); 17.1 (7.2) yrs.	SP&PP 100%; 50.4 (7.6); 60%; EDSS: 4.9 (0.9); 18.9 (9.8) yrs.	Aerobic fitness (VO2 and heart rate)	MFIS (S)	8-10	16%	9%	NR
12. Briken et al. 2014 (3) + ⁹	DE	RCT	12	11	Bicycle ergometer (aerobic)	Waitlist (TAU)	SP&PP 100%; 58.8 (6.8); 54%; EDSS: 5.0 (0.8); 13.3 (5.4) yrs.	SP&PP 100%; 50.4 (7.6); 60%; EDSS: 4.9 (0.9); 18.9 (9.8) yrs.	Aerobic fitness (VO2 and heart rate)	MFIS (S)	8-10	8%	9%	NR
13. Bulguroglu et al. 2017 (1) + ¹⁰	TU	RCT	12	13	Mat Pilates (resistive)	Relaxation and respiration exercises (TAU)	NR; 45 (39.3-49.5); NR; EDSS: 1.8 (1.1-3.3); 4.5 (3-13.3) yrs.	NR; 40 (26-43); NR; EDSS: 1 (0.5-2); 3 (1-8.5) yrs.	NR	FSS (S)	8	20%	13%	NR
14. Bulguroglu et al. 2017 (2) + ¹⁰	TU	RCT	13	13	Reformer Pilates (resistive)	Relaxation and respiration exercises (TAU)	NR; 37 (29.5-40); NR; EDSS: 2 (1-3); 5 (2-10) yrs.	NR; 40 (26-43); NR; EDSS: 1 (0.5-2); 3 (1-8.5) yrs.	NR	FSS (S)	8	13%	13%	NR
15. Çakt et al. 2010 (1) ^ ¹¹	TR	RCT	15	15	Cycling progressive resistive & balance (combined)	TAU	NR; 36.4 (10.5); 64 %; EDSS ≤ 6.0; 6: 9.2 (5.0) yrs.	NR; 35.5 (10.9); 67%; EDSS = ≤6.0; 6.6 (2.4) yrs.	10m walk test	FSS (S) SF-36 Vitality	8	6%	40%	NR

16. Çakt et al. 2010 (2) ¹¹	TR	RCT	15	15	In home exercise (resistive)	TAU	NR; 43.0 (10.2); 80%; EDSS: ≤ 6.0 = 100% 6.2 (2.2) yrs.	NR; 35.5 (10.9); 66%; EDSS ≤ 6.0: 100% 6.6 (2.4) yrs.	10 m walk test	FSS (S) SF-36 Vitality	8	3 %	40%	NR
17. Castro-Sanchez et al. 2012 ¹²	ES	RCT	36	37	Ai-Chi exercise (general)	Physiotherapist-led exercise (resistive)	NC; 46 (9.7); 72%; EDSS: 6.3 (0.8); 10.7 (9.1) yrs.	NC; 50 (12.31); 65%; EDSS: 5.9 (0.9); 11.9 (8.7) yrs.	Pain (VAS)	FSS (S) MFIS (S)	20	0%	5%	10
18. Collett et al. 2011 (1) +x ¹³	GB	RCT	20	21	Continuous cycling (aerobic)	Intermittent cycling (resistive)	40%; 52 (8); 80%; NR; 15 (8) yrs.	38%; 50 (10); 77%; NR; 11 (7) yrs.	Walking ability (2MWT)	FSS (S)	12	5%	28%	12
19. Collett et al. 2011 (2) +x ¹³	GB	RCT	20	20	Continuous and Intermittent cycling (combined)	Continuous cycling (aerobic)	38%; 55 (10); 52%; NR; 12 (11) yrs.	40%; 52 (8); 80%; NR; 15 (8) yrs.	Walking ability (2MWT)	FSS (S)	12	45%	5%	12
20. Collett et al. 2011 (3) +x ¹³	GB	RCT	21	20	Intermittent cycling (resistive)	Continuous and Intermittent cycling (combined)	38%; 50 (10); 77%; NR; 11 (7) yrs.	38%; 55 (10); 52%; NR; 12 (11) yrs.	Walking ability (2MWT)	FSS (S)	12	28%	45%	12
21. Coote et al. 2017 +x ¹⁴	IR	RCT	33	32	Exercise plus structured education (combined)	Exercise plus attention control education (combined)	82%; 43.3(9.9); 88%; 3.3 (0.3) 6.7(5.7)	84%; 41.9(9.3); 81%; 3.3(0.7); 7.0(6.1)	Walking ability (6MWT)	MFIS (S)	12	21%	13%	26
22. Dalgas et al. 2010 ¹⁵	DK	RCT	19	19	Progressive resistance training (resistive)	TAU	100%; 47.7 (10.4); 66%; EDSS: 3.7 (0.9); 6.6 (5.9) yrs.	100%; 49.1 (8.4); 62%; EDSS: 3.9 (0.9); 8.1 (6.0) yrs.	Knee extensor Maximum, Voluntary Contraction, and Functional capacity (FCS)	FSS (S) MFI-20 (S)	12	21%	16%	12
23. Dettmers et al. 2009 #+†x ¹⁶	DE	RCT	15	15	Aerobic (aerobic)	General exercise (general)	86.86 %; 45.8 (7.9); 66.66 %; EDSS: 2.6 (1.2); 8.0 (5.9) yrs.	66.66 %; 39.7 (9.1); 73.33%; EDSS: 2.8 (0.7); 6.1 (4.3) yrs.	Yes (NR)	MFIS (S)	3	44%	33%	NR
24. Dodd et al. 2011 ¹⁷	AU	RCT	39	37	Progressive resistance training (resistive)	Social programme (TAU)	100%; 47.7(10.8); 72%; NR; NR.	100%; 50.4 (9.6); 74%; NR; NR.	Walking endurance (2MWT)	MFIS (S)	10	8%	5%	12

25. Ebrahimi et al. 2015 ^18	IR	RCT	17	17	Whole body vibration (combined)	No-intervention (TAU)	100 %; 37.06 (8.42); 11%; EDSS: 3.12 (1.19); 6.5 (4.17) yrs.	100%; 40.75 (10.56); 12%; EDSS: 3.10 (0.76); 10.5 (6.4) yrs.	NR	MFIS (NR)	10	6%	12%	NR
26. Escudero-Uribe et al. 2017 (1) +^19	ES	RCT	19	18	Whole body vibration (combined)	Waitlist (TAU)	100%; 43.1 (10.2); 62.5%; EDSS: 3.0 (1.0); 10.5 (8.8) yrs.	100%; 43.0 (9.3); 77.7%; EDSS: 3.2 (1.1); 8.0 (5.4) yrs.	Fatigue (FSS, MFIS) Walking pattern (GAITRite)	FSS (P) MFIS (P)	12	16%	0	NR
27. Escudero-Uribe et al. 2017 (2) +^19	ES	RCT	18	18	Balance trainer (resistive)	Waitlist (TAU)	100%; 40.3 (8.9); 64.2%; EDSS: 3.2 (1.1); 7.4 (5.0) yrs.	100%; 43.0 (9.3); 77.7%; EDSS: 3.2 (1.1); 8.0 (5.4) yrs.	Fatigue (FSS, MFIS) Walking pattern (GAITRite)	FSS (P) MFIS (P)	12	22%	0	NR
28. Feys et al. 2017 ^20	BE	RCT	21	21	'start-to-run' (aerobic)	Waitlist (TAU)	NR; 36.6 (8.5); 95.2%; NR; 8.1 (6.1) yrs.	NR; 44.4 (8.5); 85.7%; NR; 9.2 (5.3) yrs.	Aerobic capacity (VO ₂) Walking capacity (6MWT) Functional mobility (5-STL) (MSIS-29)	FSMC (S)	12	14%	19%	NA
29. Frevel et al. 2015 +x ²¹	DE	RCT	9	9	Internet-based home training (balance)	Hippotherapy (balance)	66%; 44.3 (8.1); 77%; EDSS: 3.8 (1.5); 16.1 (11.3) yrs.	66%; 46.9 (7.6); 88%; EDSS: 3.8 (1.1); 22.3 (8.3) yrs.	Static and dynamic balance (BBS; DGI)	FSS (S) MFIS (S) HAQUAMS fatigue subscale (S)	12	11%	11%	NR
30. Gandolfi et al. 2014 +x ²²	IT	RCT	14	12	Robotic-assisted gait training (balance)	Sensory integration balance training (balance)	NR; 50.83 (8.42); 58%; EDSS: 3.96 (0.75); 13.5 (7.60) yrs.	NR; 50.1 (6.29); 90%; EDSS: 4.35 (0.67); 14.9 (8.68) yrs.	Walking speed (GAIT Rite System) and balance (BBS)	FSS (S)	6	14%	17%	4
31. Gandolfi et al. 2015 + ²³	IT	RCT	39	41	Sensory integration balance training (balance)	Conventional rehabilitation (combined)	100%; 47.21 (6.9); 71%; EDSS Median (IQR): 3.00 (2 to 4); 12.25 (7.23) yrs.	100%; 49.56 (6.85); 75%; EDSS Median (IQR): 3.66 (2.50 to 4.25); 15.24 (7.33) yrs.	Balance (BBS)	FSS (S)	5	0	0	4
32. Garrett et al. 2012 (1) + ²⁴	IR	RCT	80	71	Physiotherapist led exercise (combined)	Waitlist (TAU)	55%; 51.7 (10); 79%; NR; 9.8(7) yrs.	55%; 48.8 (11); 87%; NR; 10.6 (8.2) yrs.	Physical impact of MS (MSIS-29)	MFIS (S)	12	31%	21%	NR

33. Garrett et al. 2012 (2) + ²⁴	IR	RCT	86	71	Fitness instructor led exercise (combined)	Wait list (TAU)	49%; 50.3 (10); 68%; 55%; 48.8 (11); 87%; NR; 10.5 (6.9) yrs.	Physical impact of MS (MSIS-29)	MFIS (S)	12	22%	21%	NR	
34. Garrett et al. 2012 (3) + ²⁴	IR	RCT	77	71	Yoga (general)	Waitlist (TAU)	60%; 49.6 (10); 70%; 55%; 48.8 (11); 87%; NR; 11.6 (8) yrs.	Physical impact of MS (MSIS-29)	MFIS (S)	12	18%	21%	NR	
35. Geddes et al. 2009 ^ ²⁵	US	RCT	9	6	Home walking programme (aerobic)	Waitlist (TAU)	25%; 51.3 (40-64); NC; 34.7 (22-50); 75%; 75%; NC; NR; NR.	NR	FSS (NR)	12	11%	33%	NR	
36. Gervasoni et al. 2014 # ²⁶	IT	RCT	15	15	Treadmill training (aerobic)	Conventional training (TAU)	37.5%; 49.6 (9.4); 40%, EDSS: 5.0 (3-6.5); 14.5 (9.7) yrs.	54.6%; 45.7 (8.6); 40%, EDSS: 5.5 (3.5-6); 15.5 (10.3) yrs.	Fatigue	FSS (S)	2	0	0	NR
37. Hayes et al. 2011 + ²⁷	US	RCT	11	11	Standard exercise & supplementary high-intensity resistance training (combined)	Standard exercise (general)	NR; 48.0 (11.9); 55%; EDSS: 5.33 (1.00); 149.9 (113.8) mo.	NR; 49.7 (10.98); 60%; EDSS: 5.15 (0.97); 142.2 (87.6) mo.	NR	FSS (NR)	12	18%	9%	NR
38. Hebert et al. 2011 (1) #+^†*** ²⁸	US	RCT	12	13	Vestibular rehabilitation (balance)	Waitlist (TAU)	92%; 46.8 (0.5); 75%; 6MWT (ft): 1,335.6 (320.3); 6.5 (5.6) yrs.	92%; 50.2 (9.2); 85%; 6MWT (ft): 1,049.2 (328.9); 9.1 (7.3) yrs.	Fatigue (MFIS ≥ 45)	MFIS (P)	6	0	7%	4
39. Hebert et al. 2011 (2) #+^†*** ²⁸	US	RCT	13	13	Aerobic and stretching (aerobic)	Waitlist (TAU)	85%; 42.6 (10.2); 85%; 6MWT (ft): 1,066.1 (335.9); 5.1 (3.2) yrs.	92%; 50.2 (9.2); 85%; 6MWT (ft): 1,049.2 (328.9); 9.1 (7.3) yrs.	Fatigue (MFIS ≥ 45)	MFIS (P)	6	0	8%	4
40. Hebert et al. 2018 #²⁹	US	RCT	44	44	Balance and Eye-Movement Exercises for People with Multiple Sclerosis (balance)	Waitlist (TAU)	NR; 46.5 (8.8); 84%; EDSS: 3.50 (1.1); 8.34 (5.7) yrs.	NR; 43.0 (10.8); 86%; EDSS: 3.34 (1.1); 8.54 (7.6) yrs.	Balance, dizziness, & fatigue (CDP-SOT; MFIS ≥ 45)	MFIS (S)	14	14%	14%	NR
41. Heine et al. 2017 #†³⁰	NL	RCT	43	46	Aerobic interval training (aerobic)	MS nurse consultations (TAU)	72.1%; 43.1 (9.8); 74.4%; EDSS: 2.5 (2.0-3.5); 7.0 (2.0-10.0) yrs.	73.9%; 48.2 (9.2); 71.7%; EDSS: 3.0 (2.0-4.0); 12.0 (2.0-19.0) yrs.	Fatigue (CIS20r fatigue ≥35)	CIS20r fatigue subscale (P)	16	21%	15%	32

42. Hogan et al. 2014 (1) + ³¹	IE	RCT	66	19	Group physiotherapy (combined)	Waitlist (TAU)	27%; 57 (10); 62.5%; 33.3%; 49 (6); 86.6%; GNDS= 3 to 4 18 (9) yrs.	NR	MFIS (NR)	12	27%	21%	NR	
43. Hogan et al. 2014 (2) + ³¹	IE	RCT	45	19	Individual Physiotherapy (general)	Waitlist (TAU)	20%; 52 (11); 57.14%; GNDS= 3 & 4= 100% 13 (8) yrs.	33.3%; 49 (6); 86.6%; GNDS= 3 & 4 = 100% 10 (3) yrs.	NR	MFIS (NR)	12	22%	21%	NR
44. Hogan et al. 2014 (3) + ³¹	IE	RCT	16	19	Yoga (general)	Waitlist (TAU)	31%; 58 (8); 61%; GNDS = 3 & 4; 15 (8) yrs.	33%; 49 (6); 87%; GNDS = 3 & 4; 10 (3) yrs.	NR	MFIS (NR)	12	19%	21%	NR
45. Hugos et al. 2017 ³²	US	RCT	20	20	MS Spasticity: Take Control program (flexibility)	Stretching booklet (TAU)	52.6%; 52.8 (12.3); 68%; EDSS: 4.8 (1.1); 15.1 (8.1) yrs.	42.1%; 53.4 (12.8); 84%; EDSS: 4.9 (1.5); 15.7 (10.5) yrs.	NR	MFIS (S)	4	5%	5%	NR
46. Kalron et al. 2017 +x ³³	IL	RCT	22	23	Pilates (general)	Standard physical therapy (general)	100%; 42.9 (7.2); 68.2%; EDSS: 4.1 (1.1); 11.3 (6.9) yrs.	100%; 44.3 (6.6); 60.87%; EDSS: 4.6 (1.3); 12.4 (5.7) yrs.	NR	MFIS (NR)	12	12%	8%	NR
47. Karbandi et al. 2015 #+x ³⁴	IR	RCT	41	44	Group Yoga (general)	Individualised Yoga (general)	NR	NR	Fatigue	MFIS (NR)	6	31%	34%	NR
48. Kargarfard et al. 2012 # ³⁵	IR	RCT	16	16	Aquatic exercise (general)	TAU	100%; 33.7 (8.6); 100%; EDSS: 2.9 (0.9); EDSS: 4.9 (2.3) yrs.	100%; 31.6 (7.7); 100%; EDSS: 3.0 (0.7); 4.6 (1.9) yrs.	Fatigue	MFIS (NR)	8	37%	31%	NR
49. Kargarfard et al. 2017 # ³⁶	IR	RCT	20	20	Aquatic exercise (general)	Waitlist (TAU)	100%; 36.5 (9); 100%; EDSS: 3.4 (1.1); 6.4 (2.3) yrs.	100%; 36.2 (7.4); 100%; EDSS: 3.7 (1); 6.1 (2) yrs.	NR	MFIS (NR)	8	15%	25%	NR
50. Kerling et al. 2015 + ³⁷	DE	RCT	30	30	Endurance and resistive exercise (combined)	Endurance exercise (aerobic)	NR; 42.3 (9.0); 80%; EDSS: 2.6 (1.1); NR.	NR; 45.6 (11.4); 66.6%; EDSS: 3.1 (1.3); NR.	NR	MFIS (NR) SF-36 Vitality (NR)	12	36.6%	40%	NR
51. Kern et al. 2013 ^ ³⁸	DE	RCT	12	15	Climbing (combined)	Waitlist (TAU)	40%; 43.5 (36.5 to 47); 60%; EDSS: 5.5 (2.9 to 6.5); 15.5 (6.8 to 21) yrs.	35%; 44 (40.8 to 48.8); 71%; EDSS: 4 (2.5 to 6.0); 11 (3.5 to 14.5) yrs.	NR	WEIMuS (NR)	22	16%	6%	NA: 122 (new participants recruited)
52. Kooshiar et al. 2015 # ³⁹	IR	RCT	20	20	Aquatic exercise (general)	No intervention	75.7%; 29.2 (8.0); 100%; EDSS: 2.5 (1.1); NR.	NR.	Fatigue	FSS (NR) MFIS	8	10%	5%	NR

53. Küçük et al. 2016 +x ⁴⁰	TR	RCT	11	9	Clinical Pilates (general)	Traditional exercises (general)	NR; 47.2 (9.5); 63.6%; EDSS: 3.2 (2.2); 14.8 (7.4) yrs.	NR; 49.7 (8.9); 66.7%; EDSS: 2.8 (1.4); 14.2 (9.5) yrs.	NR	MFIS (NR)	8	NC	NC	NR
54. Learmonth et al. 2011 ^ ⁴¹	GB	RCT	20	12	Group exercise (combined)	TAU	NR; 51.4 (8.06); 75%; EDSS: 6.14 (0.36); 13.4 (6.4) yrs.	NR; 51.0 (8.0); 50%; EDSS: 5.82 (0.51); 12.6 (8.1) yrs.	Timed 25-Foot Walk Test	FSS (S)	12	15%	8%	NR
55. Learmonth et al. 2017 ^ ⁴²	US	RCT	29	28	Walking and strength programme plus behavioural change intervention based on SCT aimed at exercise participation (combined)	Waitlist (TAU)	89.6%; 48.7 (10.4); 96.5%; SR-EDSS: 1.25 (0-6); 14.8 (8.5) yrs.	89.2%; 48.2 (9.1); 96.4%; SR-EDSS: 2 (0-5.5); 13 (7.7) yrs.	Exercise behaviour (GLTQ)	FSS (S)	16	13.7%	7%	NR
56. Lutz et al. 2017 ^ ⁴³	DE	RCT	9	9	Exercise-based patient education programme. Behavioural components (general)	Waitlist (TAU)	37.5%; 52.4 (10.4); 87.5%; EDSS: 3.5 (2.25-3.5); 12.5 (10.0) yrs.	66.6%; 56.0 (7.4); 100%; EDSS: 3.5 (2.0-3.5); 17.2 (7.4) yrs.	NR	WEIMuS (S)	6	11%	33%	NA
57. McCullagh et al. 2008 ^ ⁴⁴	IE	RCT	17	13	Aerobic exercise (aerobic)	TAU	61%; 40.5 (12.68); 82%; NR; 5.4 (4.35) yrs.	52.9%; 33.58%; 77%; NR; 5 (3.52) yrs.	NR	MFIS (NR)	12	29%	7%	12
58. Mokhtarzade et al. 2017 ^ ⁴⁵	IR	RCT	25	20	interval exercise (aerobic)	No intervention	100%; 32.04 (2.81); 100%; EDSS: 1.84 (0.35); 2.69 (1.84) yrs.	100%; 31.27 (3.28); 100%; EDSS: 1.57 (0.64); 3.47 (1.26) yrs.	Cytokine expression	FSS (S)	8	12%	10%	NR
59. Mostert et al. 2002 ^ ⁴⁶	CH	RCT	19	18	Exercise training (aerobic)	No intervention (TAU)	31%; 45.23 (8.66); 77%; EDSS: 4.6 (1.2); 11 (8.5) yrs.	38%; 43.92 (13.90); 85%; EDSS: 4.5 (1.9); 12.6 (8.1) yrs.	NR	FSS (NR) SF-36 Vitality	4	31%	28%	NR
60. Negahban et al. 2013 ^ ⁴⁷	IR	RCT	12	12	Exercise therapy (general)	TAU	NR; 37 (6.69); 83%; EDSS: 3.5 (1.13); 102 (81.06) mo.	NR; 36.83 (8.74); 83%; EDSS: 3.83 (1.39); 86.58 (34.33) mo.	NR	FSS (NR)	5	0	0	NR
61. Oken et al. 2004 (1) +^ ⁴⁸	US	RCT	21	22	Recumbent bicycle training (aerobic)	Waitlist (TAU)	NR; 48.8 (10.4); NR; EDSS: 2.9 (1.7); NR.	NR; 48.4 (9.8); NR; EDSS: 3.1 (2.1); NR.	Alertness (EEG and Stroop Colour and Word Test)	MFI (S) SF-36 Vitality	26	28%	9%	NR

62. Oken et al. 2004 (2) + ⁴⁸	US	RCT	26	22	Yoga (general)	Waitlist (TAU)	NR; 49.8 (7.4); NR; EDSS: 3.2 (1.7); NR.	NR; 48.4 (9.8); NR; EDSS: 3.1 (2.1); NR.	Alertness (EEG and Stroop Colour and Word Test)	MFI (S) SF-36 Vitality	26	15%	9%	NR		
63. Ozkul et al. 2018 + ⁴⁹	TR	RCT	21	20	Aerobic and Pilates (combined)	Relaxation exercises (relaxation)	100%; 34.5 (36-43.25); 78%; EDSS: 1 (0.87-2.12); 4 (2.75-11.25) yrs.	100%; 34 (32-43.75); 78%; EDSS: 1 (1-2); 4 (2-7) yrs.	Serum concentrations	FSS (S)	8	14%	10%	NA		
64. Petajan et al. 1996 ^ ⁵⁰	US	RCT	21	25	Aerobic exercise (aerobic)	Waitlist (TAU)	NR; 41.1 (2.0); 71%; EDSS: 3.8 (0.3); 9.3 (1.6) yrs.	NR; 39.0 (1.7); 64%; EDSS: 2.9 (0.3); 6.2 (1.1) yrs.	NR	FSS (NR) POMS fatigue subscale	15	15%	11%	NR		
65. Pilutti et al. 2016 + ⁵¹	US	RCT	6	6	Recumbent cross trainer (aerobic)	Body weight supported treadmill (balance)	SP&PP 100%; 58.8 (3.0); 60%; EDSS: 7.0 (1.75); 15.2 (8.9) yrs.	SP&PP 100%; 48.2 (4.3); 40%; EDSS: 7.0 (1.5); 12.7 (11.2) yrs.	Safety as adverse event and patients experience of exercise training	MFIS (S)	12	16%	16%	NR		
66. Plow et al. 2009 +x ⁵²	US	RCT	NR	NR	Individualised rehabilitation group (general)	Group wellness intervention (EC) (PA promotion)	NR; 154. (2.3); 77%; NR; NR.	NR; 15.2 (1.9); 80%; NR; NR.	Health and physical activity; Fatigue (MFIS), QoL (SF-36), Mental health (MHI) (not fatigue-targeted)	MFIS (P)	7	NR	NR	NA		
67. Pompa et al. 2017 + ⁵³	IT	RCT	25	25	Robot-assisted gait training (general)	Conventional walking training (aerobic)	SP&PP 100%; 47 (11.17); 47.6%; EDSS: 6.62 (0.42); 17.05 (9.12) yrs.	SP&PP 100%; 49.86 (8.21); 54.4%; EDSS: 6.5 (0.49); 14.09 (5.71) yrs.	Walking capacity (2MWAT) Walking ability (FAC)	FSS (S)	4	16%	12%	NR		
68. Razazian et al. 2016 (1) + [†] ⁵⁴	IR	RCT	18	18	Aquatic exercise (general)	TAU	61.1%; 35.39 (6.89); 100%; EDSS: 3.44 (0.95); 7.11 (0.90) yrs.	66.6%; 33.11 (6.60); 100%; EDSS: 3.25 (1.24); 6.78 (0.65) yrs.	Fatigue	FSS (NR)	8	0	0	NR		
69. Razazian et al. 2016 (2) + [†] ⁵⁴	IR	RCT	18	18	Group Hatha Yoga (general)	TAU	72.2%; 33.33 (7.40); 100%; EDSS: 3.89 (1.02); 6.90 (0.90) yrs.	66.6%; 33.11 (6.60); 100%; EDSS: 3.25 (1.24); 6.78 (0.65) yrs.	Fatigue	FSS (NR)	8	0	0	NR		

70. Romberg et al. 2005 ⁵⁵	FI	RCT	56	58	Inpatient Rehabilitation programme (combined)	No intervention (TAU)	NR; 43.8 (6.3); 63%; EDSS median: 2 (IQR: 1.5 to 3.5); 6.0 (6.5) yrs.	NR; 43.9 (7.1); 65%; EDSS median: 2.5 (IQR: 2 to 3.5); 5.5 (6.4) yrs.	NR	MS Quality of Life-54 (NR)	24	16%	17%	NR
71. Sabapathy et al. 2011+ ⁵⁶	AU	RCT	6	15	Resistance exercise (resistive)	Endurance exercise (aerobic)	62.5%; 55 (7); 75%; Disease Step Score: Range 1 to 3; 10 (10) yrs.	62.5%; 55 (7); 75%; Disease Step Score: Range 1 to 3; 10 (10) yrs.	Muscular strength and endurance; Four step square test, timed up and go, six-minute walk tests, fatigue (MFIS)(not fatigue-targeted)	MFIS (P)	8	17%	26%	NR
72. Samaei et al. 2016 + ⁵⁷	IR	RCT	16	15	Eccentric exercise, downhill walking (aerobic)	Concentric exercise, uphill walking (aerobic)	100%; 33.9 (7.3); 82.3%; GNDS = 35.4 (9.1); 4.8 (3.3) yrs.	100%; 32.1 (7.6); 82.3%; GNDS = 32.1 (8.6); 4.5 (2.8) yrs.	2minWT, T25FW, TUG test, muscle strength, balance	MFIS (S)	4	5.8%	11.7%	NA
73. Sangelaji et al. 2011 ⁵⁸	IR	RCT	73	65	Rehabilitation programme (general)	TAU	NR; 40.3 (19 to 62); 33%; NR; 9.75 (NR) yrs.	NR; 39.1 (17 to 62); 33%; NR; 9.7 (NR) yrs.	NR	MSQoL-54 (NR)	12	0%	11%	NR
74. Sangelaji et al. 2014 ⁵⁹	IR	RCT	42	42	Combination exercise therapy (combined)	No intervention (TAU)	NR; 33.05 (7.68); 61%; EDSS: 0-4; NR.	NR; 32.05 (6.35); 68%; EDSS: 0-4; NR.	NR	FSS (NR)	12	17%	52%	36
75. Schulz et al. 2004 ⁶⁰	DE	RCT	15	13	Ergometer cycling (aerobic)	Waitlist (TAU)	NR; 39 (9); 73%; EDSS: 2.0 (1.4); NR.	NR; 40 (11); 61%; EDSS: 2.5 (0.8); NR.	NR	MFIS (NR) HAQUAMS (NR)	8	6%	0	NR
76. Shanazari et al. 2013 (1) + ⁶¹	IR	RCT	19	19	Aquatic exercise (general)	TAU	NR; NR; 100%; EDSS <4.5; NR.	NR; NR; 100%; EDSS <4.5; NR.	Fatigue	MFIS (P)	12	16%	16%	NR
77. Shanazari et al. 2013 (2) + ⁶¹	IR	RCT	19	19	Pilates (general)	TAU	NR; NR; 100%; EDSS <4.5; NR.	NR; NR; 100%; EDSS <4.5; NR.	Fatigue	MFIS (P)	12	16%	16%	NR
78. Siengsukon et al. 2016 + ⁶²	US	RCT	14	14	Aerobic exercise (aerobic)	Walking and stretching program (general)	71.4%; 48.9 (13.6); 78.5%; NR; 10.8 (8.4) yrs.	64.2%; 50.9 (12.2); 57%; NR; 9 (5.6) yrs.	Sleep quality (PSQI) & daytime sleepiness (ESS)	MFIS (S)	12	14%	14%	NR

79. Skjærbaek et al. 2014 + ⁶³	DK	RCT	6	5	Upper body exercise training (aerobic)	Individualized MS rehabilitation (general)	SP&PP 100%; 62.0 (5.9); NR; EDSS 6.5 to 8.0: 100% NR.	SP&PP 100%; 55.2(8.2); NR; EDSS 6.5 to 8.0 = 100% NR.	Tolerance to exercise training (drop-out rate, adherence and adverse events) and training quality (objective and subjective exercise Intensity)	FSMC (S)	4	17%	0	NR
80. Smith et al. 2012 + ⁶⁴	US	RCT	7	6	Exercise programme with MI interviewing aimed at exercise participation (general)	Exercise programme and Health coaching programme (behavioural plus exercise)	NR	NR	Exercise Adherence (sessions attended)	MPFS (S)	8 (average of 1-8)	0%	0%	NR
81. Straudi et al. 2014 ^ ⁶⁵	IT	RCT	12	12	Task oriented circuit training (aerobic)	TAU	33%; 49.92 (7.51); 58%; EDSS: 4.95 (0.61); 12.16 (6.91) yrs.	16%; 55.25 (13.82); 83%; EDSS: 4.83 (0.49); 18.25 (9.46) yrs.	NR	FSS (NR)	14	0	0	NR
82. Straudi et al. 2016 + ⁶⁶	IT	RCT	30	28	Robotic-assisted gait training (general)	Conventional walking therapy (general; recoded as aerobic)	SP&PP 100%; 52.26 (11.11); 63%; EDSS: 6.43 (0.38); 13.30 (6.55) yrs.	SP&PP 100%; 54.12 (11.44); 68%; EDSS: 6.46 (0.43); 17.77 (8.66) yrs.	Gait speed (10MWT) and endurance improvements (6MWT)	FSS (NR) SF-36 Vitality	6	16%	23%	12
83. Tallner et al. 2013 x ⁶⁷	DE	RCT	NR	NR	Exercise e-training (combined)	Waitlist (TAU)	NR; NR; NR; EDSS: 2.76 (0.85); NR.	NR; NR; NR; EDSS: NR; NR.	Quality of life and physical activity	WEIMuS (P)	12	NR	NR	NA
84. Tallner et al. 2016 ^ ⁶⁸	DE	RCT	59	67	Exercise e-training (combined)	Waitlist (TAU)	88%; 40.9 (10.4); 75%; EDSS: 2.8 (0.8); 9.8 (9.2) yrs.	85%; 40.7 (9.5); 75%; EDSS: 2.7 (0.8); 9.2 (7.2) yrs.	Quality of life	WEIMuS (S)	12	17%	12%	12
85. Tarakci et al. 2013 ^ ⁶⁹	TR	RCT	55	55	Comprehensive group exercise (combined)	TAU	63%; 41.49 (9.37); 67%; EDSS: 4.38 (1.37); 9 (4.71) yrs.	69%; 39.65 (11.18); 63%; EDSS: 4.21 (1.44); 8.42 (5.38) yrs.	Balance (BBS)	FSS (S)	12	7%	4%	NR
86. Uszynski et al. 2014 +x ⁷⁰	IR	RCT	8	9	Whole body vibrations group (combined)	Exercise group (combined)	75%; 44.4 (10.4); 75%; GNDS ≥1 = 75%; NR.	56%; 52.7 (10.5); 89%; GNDS ≥1 = 44%; NR.	NR	MFIS (NR)	8	25%	0	NR

87. Uszynski et al. 2015 + ⁷¹	IR	RCT	14	13	Whole body vibrations group (combined)	Exercise group (combined)	64%; 45.5 (38.5 to 52.3); 71%; GNDS ≥1 = 21%; NR.	39%; 54 (45.0 to 61.5); 100%; GNDS ≥1 = 38%; NR.	Isokinetic muscle strength (Isokinetic Dynamometer)	MFIS (S)	12	14%	8%	NR
88. van den Berg et al. 2006 ^ ⁷²	GB	RCT	10	9	Treadmill walking (aerobic)	Waitlist (TAU)	NR; 30 to 65; 88%; EDSS: 12.1 (3.8); NR.	NR; 30 to 65; 78%; EDSS: 12.9 (4.9); NR.	NR	FSS (NR)	7	20%	11%	NR
89. Vaney et al. 2012 + ⁷³	CH	RCT	34	33	Standard exercise & Robot assisted gait training (general)	Walking group (general)	NR; 58.23 (9.42); NR; EDSS: 5.88 (0.90); NR.	NR; 54.22 (11.28); NR; EDSS: 5.72 (1.06) NR.	QoL and wellbeing (EQ-5D; Well-Being VAS)	WEIMuS (S)	8	24%	30%	NR
90. Velikonja et al. 2010 + ⁷⁴	SI	RCT	10	10	Sports climbing (combined)	Hatta Yoga (general)	NR; Mdn: 42 (NR); NR; Mdn: 4 (NR); NR.	NR; Mdn: 41 (NR); NR; Mdn: 4.2 (NR); NR.	NR	MFIS (NR)	10	NR	NR	NR
91. Vermohlen et al. 2018 ^ ⁷⁵	DE	RCT	32	38	Hippotherapy (balance)	TAU	NR; 50 (45-53); 90%; EDSS: 4-6.5; 16.5 (11-20) yrs.	NR; 51 (47-56); 73%; EDSS: 4-6.; 17.6 (11-27) yrs.	Balance (BBS)	FSS (S)	12	6%	3%	NR
Behavioural studies														
1. Alisaleh & Shahrbano 2016 ^ ⁷⁶	IR	RCT	15	15	MBSR (CBT)	Waitlist (TAU)	NR; NR; NR; NR; NR.	NR; NR; NR; NR; NR.	Stress (C-PSS)	FSS (NR)	8	0%	0%	NR
2. Amato et al. 2014 x ⁷⁷	I	RCT	63	39	Specific cognitive attentional computer-based cognitive training	Nonspecific computer-based cognitive training placebo (Intervention/TAU)	100%; 12.0 (8.3); 80%; EDSS: 2.5 (1.3); 12.0 (8.3) yrs.	100%; 14.7 (9.2); 76%; EDSS: 3.0 (1.7); 14.7 (9.2) yrs.	NR	FSS (NR)	12	13%	15%	NR
3. Blikman et al. 2017 ♀^† ⁷⁸	NL	RCT	36	40	EC	MS nurse consultations (TAU)	76.2%; 47.7 (11.0); 81%; EDSS: 2.5 (2-4); 6.5 (3.7-17.3) yrs.	72.7%; 46.6 (11.5); 68.1%; EDSS: 1.8 (1-4); 7.5 (3-14) yrs.	Fatigue (CIS20r ≥35)	CIS20r Fatigue subscale (P)	16	14%	9%	36
4. Bogosian et al. 2015 ^ ⁷⁹	GB	RCT	19	21	MBCT adapted specifically for progressive MS (CBT)	Waitlist (TAU)	PP/SP: 100%; 53.42 (8.3); 47.4%; EDSS: 6.8 (1.6); 16.24 (10.1) yrs.	PP/SP: 100%; 50.9 (9.9); 61.9%; EDSS: 6.2 (1.4); 12.57 (8.6) yrs.	Wellbeing (GHQ)	FSS (S)	8	10%	11%	12
5. Carletto et al. 2017 + ⁸⁰	I	RCT	45	45	Body-Affective Mindfulness Intervention (CBT)	Psycho-Educational Intervention (education)	95%; 44.1 (9.4); 71%; EDSS: 2 (1); 9 (10) yrs.	80%; 45.1 (9.3); 71%; EDSS: 2.5 (2.3); 7 (7) years.	NR	FSS (S)	8	4.5%	0%	24

6. Cavalera et al. 2018 +x ⁸¹	IT	RCT	69	70	Mindfulness meditation intervention	Psycho-educational intervention (education)	94%; 42.26 (8.35); 67%; EDSS: Mdn=3; 12.64 (8.15) yrs.	92%; 43.19 (9.02); 62%; EDSS: Mdn=3; 12.24 (7.27) yrs.	QoL (MSQOL-54)	MFIS (S)	8	2%	12%	24
7. Choobforoushzadeh et al. 2015 ^ ⁸²	IR	RCT	12	12	Neurofeedback Training (neurocognitive rehab)	Neurologist (TAU)	100%; 34.28 (8.17); 50%; EDSS: 3.8 (1.5) 6.91 (4.52) yrs.	100%; 33.39 (7.72); 50% EDSS: 3.9 (1.4) 6.24 (4.3) yrs.	NR	FSS (NR)	8	0%	0%	8
8. Ehde et al. 2015 + ⁸³	US	RCT	75	88	Telephone-delivered self-management CBT and positive psychology programme for MS symptom self-management included fatigue education and EC module (CBT & EC)	Telephone-delivered education (education)	61%; 51.0 (10.1); EDSS ≥4.5 = 75%; ≥10 yrs = 49%.	51%; 53.2 (10.0); EDSS ≥4.5: 74%; ≥10 yrs = 48%.	≥50% decrease in at least one symptom: Fatigue impact (MFIS), pain interference (BPI), depression (PHQ-9)	MFIS (P)	9	13%	7%	40
9. Eyssen et al. 2013 x ⁸⁴	NL	Cluster RCT	156	113	Client-centred occupational therapy service (EC)	Occupational therapy without client-centred teaching (TAU)	39%; 44.4 (11.4); 71%; EDSS: 5.0 (1.8); 8.0 (7.8) yrs.	21%; 47.1 (9.9); 66%; EDSS: 5.1 (1.7); 8.3 (9.2) yrs.	Disability impact (DIP) Participation (IPA)	MFIS (S)	16	5%	5%	16
10. Finlayson et al. 2011 ± ⁸⁵	US	RCT	94	96	EC	Waitlist (TAU)	52%; 56 (9); 79%; NR; 15 (9) yrs.		Fatigue (FSS ≥4)	FSS (P)	7	28%	27%	24
11. Fischer et al. 2015 ^ ⁸⁶	DE	RCT	45	45	Web-based CBT integrating several approaches targeting depression (not adapted for pwMS) (CBT)	Waitlist (TAU)	47%; 45.36 (12.64); HAQUAMS: Walking ability <500m = 51%; 8.20 (7.31) yrs.	42%; 45.20 (10.56); HAQUAMS: Walking ability <500m = 49%; 8.40 (7.45) yrs.	Depression (BDI)	FSMC (S) HAQUAMS (S)	9	22%	20% (BDI only)	24

12. Flachenecker et al. 2017 + ⁸⁷	GE	RCT	14	16	Neuropsychological attention training with varying time constraint and difficulty (neurocognitive rehab)	Neuropsychological attention training without varying time constraint and difficulty (neurocognitive rehab)	43%; 43.3 (7.3); 58%; EDSS: 3.8 (1.3); 6.5 (4.0) yrs.	56%; 45.2 (7.1); 88%; EDSS: 4.7 (1.3); 9.4 (7.0) yrs.	NR	WEIMuS (NC)	2	12%	0%	NR
13. Garcia-Burguillo Aguilera-Maturana 2009 + ⁸⁸	E	CCT	9	5	EC	NR	66.7%; 44.7 (NR); 88.9%; EDSS: 2.5 (1.2); 9.5 (NR) yrs.	60%; 44.4 (NR); 80%; EDSS: 2.6 (1.3); 8 (NR) yrs.	Fatigue (FSS ≥ 3.5)	FIS Physical (NR)	10	NR	NR	NR
14. Garcia Jalon et al. 2012 + ⁸⁹	IE	RCT	13	10	EC	Peer support (education)	15%; 45.85 (9.93); 76%; RMI: 12.77 (2.12); 11 (7.01) yrs.	30%; 52 (7.01); 60%; RMI: 13.1 (1.44); 14.22 (11.94) yrs.	Fatigue (FSS ≥ 4)	FIS (S) FSS (S)	6	23%	0%	12
15. Ghahari et al. 2010 (1) + ⁹⁰	A	RCT	25/24	23/20	EC	No intervention	65%; NR; 96%; NR; 102.22 (83.38) mo.	57.1%; NR; 72%; NR; 92.59 (69.466) mo.	Fatigue (FSS ≥ 4)	FIS (P)	7	NR	NR	12
16. Ghahari et al. 2010 (2) + ⁹⁰	A	RCT	19/23	26/20	EC (EC; recoded as education)	No intervention	77.8%; NR; 82%; NR; 116.00 (85.56) mo.	57.1%; NR; 72%; NR; 92.59 (69.466) mo.	Fatigue (FSS ≥ 4)	FIS (P)	7	NR	NR	12
17. Graziano et al. 2013 + ⁹¹	I	RCT	71	73	Group CBT for depression and adjustment to MS (included a fatigue management module) (CBT)	Education; Stem cells, complementary and alternative therapies, and nourishment (education)	95%; 42.3 (8.5); 66%; EDSS: NR; 8.6 (5.2) yrs.	93%; 38.3 (10.1); 60%; EDSS: NR; 7.2 (5.3) yrs.	NR	MSQOL-54 energy subscale (NR)	8	49%	53%	16

18. Grossman et al. 2010 ^{^92}	CH	RCT	76	74	MBSR only yoga element adapted for pwMS (CBT)	TAU	79%; 45.93 (10.00); 78%; EDSS: 3.03 (1.12); 7.74 (0.90) yrs.	85%; 48.68 (10.58); 81; EDSS: 2.98 (0.83); 9.71 (0.88) yrs.	HRQOL (PQOLC; HAQUAMS), depression (CES-D), and fatigue – (MFIS)(not fatigue- targeted)	MFIS (P)	10	10%	19%	24
19. Hildebrandt et al. 2007 ^{^93}	DE	RCT	25	25	Computer-based specific cognitive training focusing on memory and working memory (neurocognitive rehab)	TAU	100%; 42.4 (25.0 to 55.0); 42%; EDSS: 2.9 (1.0 to 7.0); 5.4 (range: 0.2 to 25.6) yrs.	100%; 36.5 (23.0, 63.0); 92%; EDSS: 2.7 (0.0 to 7.0); 4.5 (range 0.2 to 20.0) yrs.	NR	FSS (NR)	8	68%	0	NR
20. Kiropoulos et al. 2016 ^{^94}	AU	RCT	15	15	Individual CBT for depression (CBT)	TAU	100%; 34.60 (9.06); 86.7%; EDSS: 100% walking independently without aid 26.20 (15.58) yrs.	100%; 39.27 (9.93); 60%; EDSS: 100% walking independently without aid 23.53 (16.06) yrs.	Depression (BDI-II)	MFIS-5 (S)	8	0%	0%	12
21. Kos et al. 2007 ^{⊕†^95}	BE	RCT	28	23	EC	Education	72%; 42.9 (9.1); 8%; MSFC: 0.13 (0.6); 6.1 (4.9) yrs.	61%; 44.5 (9.9); 8%; MSFC: 0.16 (0.7); 8.2 (9.0) yrs.	Fatigue (≥ 3 fatigue subscale GNDS)	MFIS (P) FSS (S)	7	14%	31%	24
22. Kos et al. 2016 ^{⊕+^96}	BE	RCT	17	14	EC + goals for physical activity (EC)	Relaxation therapy (relaxation)	NR; 37 (8.2); NR; EDSS: 3 (2.5- 3.25); NR.	NR; 44 (8.9); NR; EDSS: 3.5 (3.5-4); NR.	Fatigue (VAS ≥ 60)	MFIS (NR)	3	18%	21%	12
23. Mackay et al. 2015 ^{+^97}	AU	RCT	20	20	Relaxation, mindfulness, social support, and education with biofeedback (relaxation)	Relaxation, mindfulness, social support, and education (relaxation; recoded as education)	100%; 45.45 (13.34); 75%; EDSS: 2.41 (1.84); 8.29 (6.95) yrs.	100%; 15 (75%); 85%; EDSS: 2.41 (1.57); 9.07 (6.39) yrs.	NR	FSS (NR)	4 (t3)	0	0	12 (t4; not reported)
24. Mathiowetz et al. 2005/2007 ^{⊕^98,99}	US	RCT	78	91	EC	Waitlist (TAU)	61.5%; 48.3 (8.4); 83%; 33% unable to work; 9.5 (7.4) yrs.	Fatigue (FSS ≥ 4)	FIS (P)	7	21%	25%	48	

25. Mattioli et al. 2015 ¹⁰⁰	I	RCT	19	22	Specific cognitive training: attention/information processing speed, executive function and memory (neurocognitive rehab)	Non-specific cognitive Training (TAU)	100%; Median 43 (IQR: 34 to 53); 65%; Median EDSS: 2 (IQR: 1 to 3.5); Median 36 (IQR: 12 to 96) yrs.	100%; Median 45 (IQR: 38 to 50); 58%; Median EDSS: 2 (IQR: 2 to 3); Median 23.5 (IQR: 12 to 120) yrs.	NR	MFIS (NR)	31 (intervention lasted 16 weeks)	0	0	NR
26. Mohr et al. 2003 (1) Secondary data analysis of (Mohr et al. 2001) + ¹⁰¹	US	CCT	NC	NC	Individual standard CBT for depression and MS symptom management (included a module for fatigue management) (CBT)	Sertraline (medication)	NR	NR	Fatigue impact (FAI) but primary analysis was Depression (BDI)	FAI (P)	16	NC	NC	NR
27. Mohr et al. 2003 (2) Secondary data analysis of (Mohr et al. 2001) + ¹⁰¹	US	CCT	NC	NC	Supportive-expressive group therapy (emotional expression psychotherapy)	Sertraline (medication)	NR	NR	Fatigue impact (FAI); primary analysis was Depression (BDI)	FAI (P)	16	NC	NC	NR
28. Mohr et al. 2007 + ¹⁰²	US	RCT	62	65	Telephone-administered standard CBT for depression with EC module (CBT & EC)	Telephone-administered supportive emotion-focused therapy (emotional expression psychotherapy)	NR; 48.60 (9.62); 75.8%; GND: 23.89 (5.82); 11.59 (1.05) yrs.	NR; 47.35 (1.10); 78.5%; GND: 22.86 (6.69); 1.89 (1.06) yrs.	Depression (BDI; HSRD)	MFIS (NR)	16	8%	11%	NR
29. Moss-Morris et al. 2012 ¹⁰³	GB	RCT	23	22	CBT	TAU	43.5%; 40.14 (17.76); 70.6%; 41.81 (11.43); 69.6%; S-EDSS: 39.1% = 4; 21 (9.05) yrs.	94.1%; S-EDSS: 58.8% = 4; 16 (7.88) yrs.	Fatigue (CFS >4)	CFS (P) MFIS (P)	10	13%	27%	NR
30. Nazari et al. 2015 # ¹⁰⁴	IE	RCT	25	25	Relaxation	No intervention	NR any subtype defined in the inclusion criteria; 33.90 (5.60); 100%; NR; 5.18 (4.69) yrs.	NR any subtype defined in the inclusion criteria; 34.40 (7.70); 100%; NR; 4.78 (3.36) yrs.	Fatigue (FSS ≥ 4)	FSS (NR)	4	0	0	8

31. Pérez-Martín et al. 2017 ^{^105}	SP	RCT	30	32	Computer-assisted neuropsychological training program (neurocognitive rehab)	Booklet containing a set of guidelines and general advice on the influence of habits and lifestyles on cognitive functions (TAU)	90%; 44.93 (9.89); 56.3%; EDSS: 2.78 (1.98) 11.50 (8.05).	93.7%; 40.88 (8.50); 76.7% EDSS: 2.11 (1.36) 9.59 (7.40).	Several neuropsychological scales, anxiety and depression (HADS), and QoL (MSQoL-54)	FSS (NR)	12	0%	0%	NR
32. Pöttgen et al. 2018 ^{#^106}	DE	RCT	139	136	CBT	No intervention	70.5 %; 40.80 (11.12); 82%; DS: 54% ≥ moderate; 8.91 (7.47) yrs.	75%; 41.90 (9.36); 79%; DS: 53% ≥ moderate; 9.19 (7.43) yrs.	Fatigue (FSMC≥42)	CFS (P)	12	26%	11%	12
33. Rosti-Otajärvi 2013 ^{^107}	FI	RCT	60	42	Computer-based cognitive training as part of neuropsychological rehabilitation (neurocognitive rehab)	No intervention / TAU	100%; 43.7 (8.7); 78%; EDSS: 0-4 = 94%; 9.4 (6.9) yrs.	100%; 45.5 (9.4); 82%; EDSS: 0-4 = 93%; 10.4 (7.7) yrs.	Self-perceived cognitive deficits (PDQ)	FSMC (NR)	37 (intervention lasted 13 weeks)	4%	5%	48
34. Seebacher et al. 2015 (1) ^{^108}	GB	RCT	10	10	Motor imagery with rhythmically accentuated music and verbal cueing (bio/ neurofeedback training)	Appointment with a physician (TAU)	NR; 47.3 (CIs 95% 38.4, 56.2); 100%; EDSS: 3 (CIs 95% 1.5, 4.5); NR.	NR; 46.1 (CIs 95% 39.8, 52.5); 50%; EDSS: 2.5 (CIs 95% 1.5, 4.0); NR.	Fatigue impact	MFIS (P)	4	0	0	NR
35. Seebacher et al. 2015 (2) ^{^108}	GB	RCT	10	10	Motor imagery with metronome cues and verbal cueing (bio/ neurofeedback training)	Appointment with a physician (TAU)	NR; 41.8 (CIs 95% 34.8, 48.8); 70%; EDSS: 2.5 (CIs 95% 1.5, 4.5); NR.	NR; 46.1 (CIs 95% 39.8, 52.5); 50%; EDSS: 2.5 (CIs 95% 1.5, 4.0); NR.	Fatigue impact	MFIS (P)	4	0	0	NR

36. Seebacher et al. 2016 (1) ¹⁰⁹	A	RCT	38	38	Motor imagery with rhythmically accentuated music and verbal cueing (bio/ neurofeedback training)	TAU	NR; 43.8 (CIs 95% 39.5, 42.1); 74%; EDSS: 2.0 (CIs 95% 1.5, 4.5); NR.	NR; 43.1 (CIs 95% 39.1, 47.1); 94%; EDSS: 2.0 (CIs 95%, 1.5, 4.5); NR.	Fatigue impact	MFIS (S) SF-36 Vitality	4	11%	13%	NR
37. Seebacher et al. 2016 (2) ¹⁰⁹	A	RCT	36	38	Motor imagery with metronome cues and verbal cueing (bio/ neurofeedback training)	Regular appointments with physicians (TAU)	NR; 45.4 (CIs 95% 41, 49.8); EDSS: 2.0 (CIs 95% 1.5, 4.5); NR.	NR; 43.1 (CIs 95% 39.1, 47.1); 94%; EDSS: 2.0 (CIs 95%, 1.5, 4.5); NR.	Fatigue impact	MFIS (S) SF-36 Vitality	4	6%	13%	NR
38. Sgoifo et al. 2017 ^{#110}	I	RCT	24	24	Integrated Imaginative Distention Therapy (bio/neurofeedback training)	Waitlist (TAU)	83%; NR; NR; EDSS: 3.15 (1.97); 8.2 (7.3) yrs.	91%; NR; NR; EDSS: 3.44 (2.01); 10.5 (8.5) yrs.	Fatigue	MFIS (P)	8	4%	0%	NR
39. Simpson et al. 2017 ¹¹¹	UK	RCT	25	25	MBSR group programme excluding day retreat at week six (CBT)	Waitlist (TAU)	88%; 43.6 (10.7); 92%; EDSS: 4.5 (1.8); 8.9 (8.5) yrs.	72%; 46.3 (11.1); 88%; EDSS: 4.3 (1.7); 9.6 (9.4) yrs.	Perceived stress (PSS) and QoL (EQ-5D-5 L)	MFIS (S)	8	16%	16%	12
40. Sterz et al. 2013 ¹¹²	DE	CCT	37	32	Art therapy as part of inpatient rehabilitation (emotional expression psychotherapy)	Audio CD of relaxing music as part of inpatient rehabilitation (TAU)	NR; 37.3 (8.8); 67.6%; EDSS: 3.43; 3.4 (NR) yrs.	NR; 36.9 (9.6); 71.9%; EDSS: 3.38; 3.3 (NR) yrs.	QoL (HALEMS)	HALEMS (P) WEIMuS (NR)	3-8	NC	NC	24
41. Sutherland et al. 2005 ¹¹³	AU	RCT	14	12	Autogenic training (relaxation)	TAU	NR; 43.55 (9.47); 63.6%; EDSS: NR; 9.36 (6.28) yrs.	NR; 40.82 (6.08); 81.8%; EDSS: NR; 6.45 (2.94) yrs.	NR	POMS-SF Fatigue (NR) MSQOL-54 energy subscale (NR)	8 (2 prior to end of programme)	21%	8%	NR
42. Tesar et al. 2005 ¹¹⁴	A	RCT	10	9	Specific neuropsychological training as part of outpatient rehabilitation	Rehabilitation only (TAU)	70%; 45.3 (9.2); 70%; EDSS: 4.5 (1.7); 8 (4.2) yrs.	67%; 46.9 (11.2); 55.6%; EDSS: 4.4 (1.9); 10.4 (7.1) yrs.	NR	MFIS (NR)	4	0%	0%	12

							(neurocognitive rehab)								
43. Thomas et al. 2013 / 2014 ✉+115, 116	GB	RCT	84	80	CBT & EC	Current local practice / TAU	43%; 48.0 (10.2); 73%; APDDS: 78% ≥ 4; 40% 1 to 5 yrs.	51%; 50.1 (9.1); 73%; APDDS: 81% ≥ 4; 27% 1 to 5 yrs.	Fatigue (FSS >4)	FAI (P)	10	15%	6%	52	
44. van den Akker et al. 2017 ✉+†117	NL	RCT	44	47	CBT	MS nurse consultations (TAU)	72.7%; 50.6 (8.3); 70.5%; EDSS: 3.0 (2.8; 3.6); 8.2 (2.9-14.2) yrs.	74.5%; 46.4 (11.6); 83%; EDSS: 2.5 (2.3; 3.0); 5.2 (2.1-1.5) yrs.	Fatigue (CIS20r fatigue ≥35)	CIS20r fatigue (P)	16	7%	17%	36	
45. van Kessel et al. 2008 ✉+118	NZ	RCT	35	37	CBT	Relaxation (relaxation)	66%; 42.89 (9.92); 80%; EDSS: 3.04 (1.78); 5.54 (4.80) yrs.	49%; 47.03 (9.45); 70%; EDSS: 3.86 (1.53); 6.65 (5.91) yrs.	Fatigue (CFS ≥4)	CFS (P) WSAS (S)	8	2%	5%	24	
46. van Kessel et al. 2015 ✉+ ¹¹⁹	NZ	RCT	19	20	CBT	CBT without email support (CBT; recoded as education)	79%; 42.95 (8.16); 58%; EDSS: 42% ≥ 4.5; 4.78 (4.36) yrs.	55%; 45.70 (8.39); 90%; EDSS: 50% ≥ 4.5; 5.12 (4.29) yrs.	Fatigue (CFS ≥ 4)	CFS (P) MFIS (P)	10	21%	55%	NR	
Combined studies															
1. Bombardier et al. 2008 ¹²⁰	US	RCT	70	60	Telephone Counselling for Health Promotion using MI techniques (behavioural techniques and PA)	Waitlist (TAU)	70%; 47.5 (41 to 54); 76%; NR; 6.3 (3.4 to 10.5) yrs.	75%; 45 (40.5 to 52); 80%; NR; 6.4 (2.8 to 13.1) yrs.	Health promotion behaviours (HPLP II)	MFIS (S)	12	2.8%	15%	NR	
2. Carter et al. 2014 ¹²¹	GB	RCT	60	60	Pragmatic exercise and CBT techniques targeting confidence and self-directed exercise adapted for pwMS (behavioural plus exercise)	TAU	85%; 45.7 (9.1); 72%; EDSS: ≥4.5 = 53%; 8.4 (7.4) yrs.	78%; 46.0 (8.4); 72%; EDSS: ≥4.5 = 52%; 9.2 (7.9) yrs.	Self-reported exercise behaviour (GLTEQ)	MFIS (S) Energy subscale of MSQoL-54 (S)	12	10%	12%	24	

3. Craig et al. 2003 ^122	GB	RCT	20	21	Intravenous methyl-prednisolone and MDT intervention - physiotherapy and occupational therapy: balance. (physical rehab)	Intravenous methyl-prednisolone only (TAU)	NR; 38 (8.72); 55%; EDSS: ≥4 = 70%; 7.42 (6.94) yrs.	NR; 42 (11.09); 80%; EDSS: ≥4 = 75%; 5.69 (5.09) yrs.	Neurological disability (GND)	SF-36 vitality (S)	4	0	4%	12
4. Di Fabio et al. 1998 ^123	US	RCT	20	26	MDT rehabilitation: physiotherapy and occupational therapy and balance (physical rehab)	Waitlist (TAU)	PP/SP: 100%; 49 (12); 75%; EDSS 5 to 8 = 100%; 17 (10) yrs.	PP/SP: 100%; 50 (12); 73%; EDSS 5 to 8 = 100%; 15 (12) yrs.	NR	MS-RS (P)	48	35%	45%	NR
5. Ennis et al. 2006 ^124	GB	RCT	34	30	MDT health promotion education intervention, incorporating behavioural, physical activity, and exercise information (behavioural plus exercise)	Waitlist (TAU)	50%; 45 (9); 63%; EDSS: >3.5 = 78%; 7 (5) yrs.	40%; 46 (8); 63%; EDSS: >3.5 = 78%; 8 (6) yrs.	Health promotion behaviours (HPLP II)	SF-36 vitality (NR)	8	8%	0	NA: 12 (treatment group only)
6. Grasso et al. 2017 +^125	I	RCT	17	17	MDT rehabilitation plus computer assisted cognitive training (neurocognitive rehab)	MDT rehabilitation plus additional occupational therapy and non-specific computer training (physical rehab)	47.1%; 59.55 (7.2); 64%; EDSS: 7.54 (0.8); 21.64 (9.4) yrs.	47.1%; 58.67 (10.3); 64%; EDSS: 7.5 (0.8); 21.9 (6.9) yrs.	HRQOL and (SF-36) depression (ADRS)	Vitality (SF-36) (NR)	12	5%	0%	12
7. Hugos et al. 2010 ♦^126	US	RCT	21	20	Fatigue: Take Control (behavioural plus exercise)	Waitlist (TAU)	NR; 55.41 (9.10); 87%; EDSS: 4.9 (1.2); 14.24 (7.04) yrs.	NR; 55.41 (9.10); 73%; EDSS: 5.5 (0.8); 15.54 (6.52) yrs.	Fatigue	MFIS (P) FSS (S)	8	25%	25%	13
8. Hugos et al. 2018/2019 ♦+^127, 128	US	RCT	109	109	Fatigue: Take Control (behavioural plus exercise)	MS: Take Control (education)	61%; 53.9 (9.8); EDSS: 5.1 (1.1); 12.3 (7.6) yrs.	55%; 53.6 (10.5); EDSS: 5.3 (1.1); 12.7 (9.3) yrs.	Fatigue (MFIS≥25)	MFIS (P)	6-10	9%	9.5%	24 (48 at one site only)

9. Nedeljkovic et al. 2016 [#] ¹²⁹	RS	RCT	19	20	Methylpred. & Aerobic exercise & MDR (physical rehab)	Methylpred. & TAU	100%; 41.7 (9.5); 63.2%; EDSS: 4.4 (1.3); 8 (3-13) yrs.	100%; 39.7 (10.5); 70%; EDSS: 4.2 (0.7); 5 (2-10.8) yrs.	Fatigue	FSS (NR)	4	13.6%	17%	12
10. O'Hara et al. 2002 [#] ¹³⁰	GB	RCT	80	103	Discussion of individual's self-care physical (e.g. mobility and exercises), social and psychological strategies, e.g. coping with stress information booklet (behavioural plus exercise)	TAU	44%; 52.5(11.2); 71%; GT: 5.8; 11.3(7.6) yrs.	51%; 50.4 (10.4); 68%; GT: 5.8; 12.2 (9.2) yrs.	Mobility (BI), QoL (SF-36), Need for assistance with daily activities (SDDR)	SF-36 vitality (NR)	24 (intervention lasted 4 weeks)	9%	7%	NR
11. Patti et al. 2002 ⁺ ¹³¹	I	RCT	58	53	MDT outpatient rehabilitation (physiotherapy and occupational therapy and general exercise) (physical rehab)	Self-directed exercise program (general)	NR; 45.2 (12.0); 59%; EDSS: 6.2 (1.2); 17.2 (8.1) yrs.	NR; 46.1(6.0); 57%; EDSS: 6.1 (1.2); 17.2 (4.8) yrs.	QoL (SF-36) Neurological impairment (EDSS)	FIS (S) SF-36 Vitality (P)	6	0	0	NA
12. Rietberg et al. 2014 [#] ¹³²	NL	RCT	23	25	Aerobic exercise & EC (behavioural plus exercise)	Nurse consultation / TAU (education)	70%; 45 (9.9); 61%; EDSS: 3 (3); 7 (6.6) yrs.	48%; 47 (8.6); 68%; EDSS: 4 (2); 8 (6.1) yrs.	Fatigue (according to MSCCPG definition)	CIS-20R (P) FSS (S) MFIS (S)	12	9%	8%	12
13. Pilutti et al. 2014 [#] ¹³³	US	RCT	41	41	Behavioural intervention (self-monitoring, goal setting, pedometer and activity logs, one-on-one web-based video coaching) to increase physical activity (PA promotion)	Waitlist (TAU)	24%; 48.4 (9.1); 73%; NR; 10.6 (7.1) yrs.	17%; 49.5 (9.2); 78%; NR; 13.0 (9.1) yrs.	NR	FSS (NR) MFIS (NR)	24	8%	5%	NR

14. Storr et al. 2006 ^{^134}	DK	CCT	41	65	MDT Service (Physiotherapy and Occupational Therapy) (physical rehab)	Waitlist (TAU)	13%; 53.09 (8.92); 58%; EDSS 6.5 (3.5 to 8.0); 9.0 (1 to 23) yrs.	23%; 50.19 (9.98); 69%; EDSS: 6.5 (1.5 to 8.0); 9.0 (0 to 37) yrs.	HRQoL (FAMS)	VAS (S)	3-5	8%	26%	NR
15. Stuijbergen et al. 2003 ^{^135}	US	RCT	76	66	Wellness Programme (Educational and skill-building for lifestyle change) (behavioural plus exercise)	Waitlist (TAU)	NR; NR; NR; EDSS: 14.9 (7.1) NR.	NR; NR; NR; EDSS: 16.4 (8.6) NR.	QoL (SF-36)	SF-36 vitality (P)	20 (intervention lasted 8 weeks + telephone follow-up for 12 weeks)	26%	14%	32
16. Thomas et al. 2017 ^{^136}	UK	RCT	15	15	Mii-vitalise BCT components with general exercise (behavioural plus exercise)	Waitlist (TAU)	80%; 50.9 (8.08); 93%; APDDS:4.1(1.2); NR.	60%; 47.6 (9.26); 87%; APDDSL4.3(1.1); NR.	NR	FSI (S)	48	7%	0	NR
17. Turner et al. 2016 ^{⊕+^137}	US	RCT	31	33	General (land-based) exercise & MI (behavioural plus exercise)	Exercise DVD & booklet / TAU (education)	70%; 53.6 (13.1); 42%; Mobility PF: 2.73 (1.35) 11.85 (10.41) yrs.	65%; 52.7 (11.6); 29%; Mobility PF: 2.35 (1.50) 11.33 (9.00) yrs.	Fatigue (MFIS ≥ 20)	MFIS (P)	6	3%	0	18
18. Zalisova et al. 2001 ^{⊕x^138}	CZ	RCT	9	9	Aerobic exercise & Relaxation (behavioural plus exercise)	No intervention	NR; 36.6 (6.64); 6%; AI: 3.27 (1.71); 6.8 (6.19) yrs.	NR; 38.87 (6.98); 0%; AI: 3.5 (1.65); 17.1 (3.8) yrs.	Fatigue (self-reported fatigue)	MFIS (NR)	6	0	0	NR

*Informed by the aims of the intervention when primary and secondary outcomes have not been clearly reported by the author.

**Mixed sample with MS subgroup.

***Long-term follow-up (12 months) data provided for one site

†Participants were excluded if they had major depression or insufficient motivation to participate in additional training along with the normal rehabilitation program.

‡ Participants with limited standing balance were included

+ Head-to-head comparison of exercise, behavioural, or combined interventions (including comparisons of the same treatment type).

^Included in the post-treatment pairwise meta-analysis (inclusive of assessments taken up to 3 months).

^x No available data for pairwise or network meta-analyses.

[⊕] Fatigue-targeted intervention: described and evaluated in-depth elsewhere (¹³⁹ / PROSPERO (Protocol ref. CRD42016033763)).

Abbreviations:

10MWT (10 Meter Walking Test); 2MWT (2 Minute Walking Test (minutes)); 6MWT (6 Minute Walking Test); ADRS (Asberg Depression Rating Scale); AI (Ambulation Index); APDDS (Adapted Patient Determined Disease Steps); BBS (The Berg Balance Scale); BDI (Beck Depression Inventory); BI (Barthel Index); BPI (Brief Pain Inventory); CBT (Cognitive behavioural therapy); CCT (Controlled Clinical Trial); CES-D (Center for Epidemiologic Studies Depression Scale); CIS-20R (Checklist Individual Strength Fatigue total score); C-PSS (Cohen Perceived Stress Scale); Ctrl. (Control group); Ctrl (Control group); DASS (Depression Anxiety and Stress Scale); DGI (Dynamic Gait Index); DIP (Disability and Impact Profile); DS (Disease Steps);

EC (Energy Conservation); EE (Energy Effectiveness); EDSS (Expanded Disability Status Scale); Exp (Experimental group); FAMS (Functional Assessment of Multiple Sclerosis); FCS (Functional Capacity Score); GHQ (General Health Questionnaire); GLTEQ (Godin Leisure Time Exercise Questionnaire); GNDS (Guy's Neurological Disability Scale); GT (Guttman type scale); HALEMS and HAQUAMS (Hamburger Quality of life in MS questionnaire); HPLP II (Health-Promoting Lifestyle Profile II); HRQoL (Health related quality of life); HSRD (Hamilton Rating Scale for Depression); IPA (Impact on Participation and Autonomy); MBCT (Mindfulness-Based Cognitive Therapy); MBSR (Mindfulness-based Stress Reduction); MDR (multidisciplinary rehabilitation); MDT (Multidisciplinary); MHI (Mental Health Inventory); MI (Motivational interviewing); mo (Months); Mobility PF (Mobility item of the Performance Scales); MSCCPG (The Multiple Sclerosis Council for Clinical Practice Guidelines); MSFC (Multiple Sclerosis Functional Composite Score); MSIS-29 (Multiple Sclerosis Impact Scale- 29); MSQOL-54/ -R (Multiple Sclerosis Quality of Life 54 / revised); MS-RS (MS-Related Symptom Checklist); NA (Not applicable); NC (Not clear from text); NR (Not reported); PA (Physical activity promotion); PDQ (Perceived Deficits Questionnaire); PHQ-9 (The Patient Health Questionnaire version 9); PP (Primary Progressive); PQOLC (German-language Profile of Health-Related Quality of Life in Chronic Disorders); PSS (Perceived Stress Scale-10 items); QoL(Quality of Life); RCT (Randomised Controlled Trial); RMI (Rivermead Mobility Index); RR (Relapsing Remitting MS); SDDR (Standard Day Dependency Record); S-EDSS (Self-report Expanded Disability Status Scale); SF-12 (Short-form 12 Health Survey); SF-8 (Short-form 12 Health Survey); SP (Secondary Progressive MS); TAU (Treatment as usual/standard care); yrs (Years).

Self-report Fatigue Scales:

1. CFS: Chronic Fatigue Scale
2. FIS: Fatigue Impact Scale
3. GFS: Global Fatigue Severity subscale of the FAI
4. FSMC: Fatigue Scale of Motor and Cognition
5. FSS: Fatigue Severity Scale
6. MFIS: Modified Fatigue Impact Scale and 5-item version (MFIS-5)
7. MPFS: Mental and Physical Fatigue Scale
8. POMS-SF: Short form of the Profile of Mood States: Fatigue subscale.
9. SF-36 Vitality: Short-form 36 Health Survey vitality subscale
10. SF-8VT: Short-form 8 Health Survey vitality subscale
11. WEIMuS: Würzburg Fatigue Inventory in MS
12. WSAS: Work and Social Adjustment Scale

Supplementary Table B2: Template for intervention Description and Replication (TiDiER) characteristics for exercise treatments (emboldened studies were significantly effective at post-treatment in pairwise meta-analyses)

Study reference	Theory/ rationale	Who delivered (level of training)	Timing & Mode of Delivery (week x frequency x minutes (mode))	Intensity	Setting (format: Homework)	Tailoring	Adherence Assessed	Fidelity Assessed	Exercise components			
									Aerobic	Resistive	Flexibility	Balance
			Exp. / Ctrl.									
General Exercise												
1. Ahmadi et al. 2013 (2) ¹	Exp.	No	Physiotherapist (NR)	8 x 3 x 60-70 (face-to-face)	40-75% age predicted maximal HR	Physiotherapy clinic (NR)	Yes	NR	NR	✓	✓	✓
2. Atri et al. 2012 ³	Exp.	No	NR	8 x 3 x 45	NR	Community (group: NR)	NR	NR	NR	✓	✓	✓
3. Azimzade et al. 2013 ⁵	Exp.	No	Researcher (under supervision of Experienced Tai Chi instructor)	(Face-to-face) 12 x 2 x 60 (face-to-face)	NR	NR (NR: NR)	No	NR	NR	✓	✓	✓
4. Castro-Sanchez et al. 2012 ¹²	Exp.	No	Physiotherapist (NR)	20 x 2 x 60 (face-to-face)	NR	Swimming pool (group: NA)	Yes	NR	NR	✓	✓	✓
5. Dettmers et al. 2009 ¹⁶	Ctrl.	No	1 x Physical education student (Master's degree)	3 x 3 x 45	NR	Rehabilitation Unit (group: NR)	Yes	NR	NR	✓	✓	
6. Garrett et al. 2012 (2) ²⁴	Exp.	No	Yoga instructor accredited by the Yoga Federation of Ireland	(Face-to-face) 10 x 1 x 60 (face-to-face)	N/A	Community (group)	No	NR	NR	✓	✓	✓
7. Hayes et al. 2011 ²⁷	Ctrl.	No	NR	12 x 3 x 60 (face-to-face)	NR	NR	No	Yes	NR	✓	✓	✓
8. Hogan et al. 2014 (2) ³¹	Exp.	No	Physiotherapist (manual and instruction)	10 x 1 x 60 (face-to-face)	NR	Community (one to one: NA)	Yes	Yes	Yes	✓	✓	✓
9. Hogan et al. 2014 (3) ³¹	Exp.	No	Yoga instructor (NR)	10 x 1 x 60 (face-to-face)	NR	Community (group: NA)	Yes	Yes	Yes	✓	✓	✓
10. Kalron et al. 2017 ³³	Exp.	No	Physical therapists (certified in Pilates method)	12 x 1 x 30 (face-to-face)	NR	MS centre + home-based (group + individual)	Yes	NR	NR	✓	✓	✓
11. Kalron et al. 2017 ³³	Ctrl.	No	Physical therapists	15min individualised home program 12 x 1 x 30 (face-to-face)		MS centre + home-based (group + individual)	Yes	NR	NR	✓	✓	✓

12. Karbandi et al. 2015 ³⁴	Exp.	No	1 x Experienced coach (NR)	6 x 2 x 10-15 (face-to-face VCD and booklet)	N/A	Community (group: NR)	NR	Yes	NR	✓	✓	✓
13. Kargarfard et al. 2012 ³⁵	Exp.	No	1 x Certified Aquatic Instructor (experience of working with people with physical disability)	8 x 3 x 60 (face-to-face)	50% - 75% maximal HR	Research Centre (group: NR)	NR	NR	NR	✓	✓	✓
14. Kargarfard et al. 2017 ³⁶	Exp.	No	Aquatic trainer (certified as water safety instructor) Neurologic physiotherapists (NR)	aquatic exercise: 8 x 3 x 60 (face-to-face) education sessions: 8 x 2-3 x 30-40 (face-to-face)	50-75% estimated maximal HR	Swimming pool (group: NA) NR	Yes	NR	NR	✓	✓	✓
15. Kooshiar et al. 2015 ³⁹	Exp.	No	2 x Physiotherapists (NR)	8 x 3 x 25-45 (face-to-face)	Tailored to individual's disability & activity level	Community (group: NR)	Yes	NR	NR	✓	✓	✓
16. Küçük et al. 2016 ⁴⁰	Exp.	No	Physiotherapist (NR)	8 x 2 x 45-60 (face-to-face)	NR	NR (group)	Yes	NR	NR	✓	✓	✓
17. Küçük et al. 2016 ⁴⁰	Ctrl.	No	NR	8 x 2 x nr (nr)	NR	NR	NR	NR	NR	✓	✓	✓
18. Lutz et al. 2017 ⁴³	Exp.	Yes	1 x Sport Scientist 1 x Assistant	6 x 2 x 60-90 (theory: practice 40:60) 2 x booklets with theoretical background& practical information	NR	NR (group: home-based individual)	Yes	Yes	NR	✓	✓	✓
19. Negahban et al. 2013 ⁴⁷	Exp.	No	Physiotherapist (NR)	5 x 3 x 30 (face-to-face)	Aerobic: 60-80% of the maximal heart rate Straight leg raising: 60% and 70% of maximal voluntary contraction Resistance: > 40% tolerated maximum load	NR (NC: NC)	Yes	NR	NR	✓	✓	✓
20. Oken et al. 2004 (2) ⁴⁸	Exp.	No	Yoga teacher following discussion with neurologist	26 x 1 x 90 (face-to-face)	NR	NR (NR: NC)	Yes	NR	Yes	✓	✓	✓
21. Patti et al. 2002 ¹³¹	Ctrl.	No	Therapist (NR)	12 x 3 x 30	NR	NR	Yes	Yes	NR	✓	✓	✓

22. Plow et al. 2009 ⁵²	Exp.	No	Therapist (NR)	Clinic: 4 sessions during 8 weeks x NR (face-to-face) home: 8 x 5 x 45 (individual)	NR	Clinic (one to one: home-based)	Yes	NR	NR	✓	✓	✓	✓
23. Razazian et al. 2016 (1) ⁵⁴	Exp.	No	1 x Certified Instructor (NR)	8 x 3 x 60 (face-to-face)	NR	Rehabilitation Centre of Hospital (group: NR)	NR	NR	NR	✓	✓	✓	✓
24. Razazian et al. 2016 (2) ⁵⁴	Exp.	No	1 x Certified Yoga Instructor (Hatha Yoga)	8 x 3 x 60 (face-to-face)	N/A	Gym Hall of Hospital (group: NR)	NR	NR	NR	✓	✓	✓	✓
25. Sangelaji et al. 2011 ⁵⁸	Exp.	No	Physiotherapist (NR)	12 x 3 x 120-180 (face-to-face)	NR	Rehabilitation centre (NR: NC)	No	NR	NR	✓	✓	✓	✓
26. Shanazari et al. 2013 (1) ⁶¹	Exp.	No	NR	12 x 3 x 60 (face-to-face)	Gradual increase in level of exercise	NR (group: NR)	NR	NR	NR	✓	✓	✓	✓
27. Shanazari et al. 2013 (2) ⁶¹	Exp.	No	NR	12 x 3 x 60 (NR)	Gradual increase in level of exercise	NR (group: NR)	NR	NR	NR	✓	✓	✓	✓
28. Siengsukon et al. 2016 ⁶²	Ctrl.	No	NA	12 x 3 x 60-70 (NR)	low-intensity exercise: below 40% of HR reserve.	NR (NR: NA)	Yes	NR	NR	✓	✓	✓	✓
29. Skjærbaek et al. 2014 ⁶³	Ctrl.	No	Physiotherapist	10 x 18 (face-to-face) (4 weeks)	65%-75% of VO2 peak Borg scale	Inpatient rehabilitation hospital (NR: None)	Yes	NR	NR	✓	✓	✓	✓
30. Smith et al. 2012 ⁶⁴	Exp	No	Physiotherapist (NR)	8x3x (15-60) (face-to-face)	NR	NR (group, NR)	NR	Yes	NR	✓	✓	✓	✓
31. Straudi et al. 2016 ⁶⁶	Exp.	No	NR	6 x 2 x 30 (face-to-face)	NA	MS treatment centre (NR: NA)	NR	NR	NR	✓	✓	✓	✓
32. Straudi et al. 2016 ⁶⁶	Ctrl.	No	NR	6 x 2 x 55 (face-to-face)	NR	Community treatment centres (NR: None)	Yes	NR	NR	✓	✓	✓	✓
33. Vaney et al. 2012 ⁷³	Exp.	No	Physiotherapist (NR)	8 x 7 x 150 + 9 sessions x 30min of Lokomat training (face-to-face)	50% body weight support in Lokomat training	Inpatient rehabilitation clinic (Individual & group: NR)	Yes	Yes	NR	✓	✓	✓	✓

34. Vaney et al. 2012 ⁷³	Ctrl.	No	Physiotherapist (NR)	9 x 30 (face-to-face)	NR	Gym room and outside (group: NR)	Yes	NR	NR	✓	✓	✓	✓
35. Velikonja et al. 2010 ⁷⁴	Ctrl.	No	Yoga Instructor (Licenced)	10 x 1 x NR (face-to-face)	NR	Rehabilitation Institute Facilities (NR)	Yes	No	No	✓	✓	✓	✓
Aerobic													
36. Ahmadi et al. 2013 (1) ¹	Exp.	No	NR (NR)	8 x 3 x 30 (face-to-face)	40-75% age predicted maximal heart rate	NR (NR)	Yes	NR	NR	✓	✓		
37. Bansi et al. 2012 ⁶	Ctrl.	Yes	Physiotherapist (NR)	5 x 5 x 30 (face-to-face)	NR	NR	No	NR	NR	✓			
38. Briken et al. 2014 (1) ⁹	Exp.	No	Physiotherapist (N/A)	8-12 x 2-3 X 15-45 (face-to-face)	Individual Aerobic threshold of 120% of and 130%.	Research Centre (NR)	Yes	Yes	NR	✓	✓		
39. Briken et al. 2014 (2) ⁹	Exp.	No	Physiotherapist (N/A)	8-12 x 2-3 X 15-45 (face-to-face)	Individual Aerobic threshold of 120% of and 130%.	Research Centre (NR)	Yes	Yes	NR	✓	✓		
40. Briken et al. 2014 (3) ⁹	Exp.	No	Physiotherapist (N/A)	8-12 x 2-3 X 15-45 (face-to-face)	Individual Aerobic threshold of 120% of and 130%.	Research Centre (NR)	Yes	Yes	NR	✓	✓		
41. Collett et al. 2011 (1) ¹³	Exp.	No	Exercise professional (NR)	Research centre: 18 sessions over 12 weeks x 20 (face-to-face) Community/home: 18 sessions over 12 weeks x 20	45% workload	Research centre & community fitness class (one to one and individual)	No	Yes	Yes	✓			
42. Dettmers et al. 2009 ¹⁶	Exp.	No	1 x Physical education student (Master's degree)	3 x 3 x 45 (Face-to-face)	NR	Rehabilitation Unit (group: NR)	Yes	NR	NR	✓	✓	✓	

43. Feys et al. 2017 ²⁰	Exp.	No	Project researcher (MSc exercise physiology, PhD)	12 x 3x (30-60) via email. Including 2 (face-to-face group sessions)	Ranging from walking ($\pm 5\text{km/h}$) to running ($\pm 10 \text{ km/h}$)	Home-based (individual)	Yes	Yes	Yes	✓
44. Geddes et al. 2009 ²⁵	Exp.	No	NR	12 x 3 x 25-40 (Individual)	At or below THR range	Home-based (individual)	Yes	Yes	NR	✓
45. Gervasoni et al. 2014 ²⁶	Exp.	No	NR	2 x 6 x 45	11 -12 of RPE	NR	Yes	NR	NR	✓ ✓ ✓ ✓
46. Hebert et al. 2011 (2) ²⁸	Ctrl.	No	1 x Physical therapist (12 yrs experience in treating MS patients)	(a) 6 x 2 x 40 (Face-to-face) (b) 10 x 7 x 40 (Home-based)	65% to 75% of HR peak	(a) Research Centre (NR: NR) (b) Home-based (individual: NA)	Yes	Yes	NR	✓ ✓
47. Heine et al. 2017 ³⁰	Exp.	Yes	1 x Physical therapist (experienced in treating MS patients)	16 x 3 30 (excl. warm-up/cool down) (Face-to-face + home-based)	Exercise intensity was based in % peak power	(a) Study Centre (individual: NR) (b) Home-based (individual: NA)	Yes	Yes	NR	✓
48. Hugos et al. 2018/2019 ^{127, 128}	Exp.	No	1 x Different MS professionals with at least one year of experience	6 x 1 x 120 (face-to-face: Manual and DVD)	NR	Academic medical centre MS clinics (group: yes)	Yes	Yes	Yes	✓
49. Kerling et al. 2015 ³⁷	Ctrl.	No	Sport scientist (NR)	12 x 2 x 40 (face-to-face)	Aerobic: 50% max workload	Institute of sports sciences (NR)	Yes	NR	NR	✓
50. McCullagh et al. 2008 ⁴⁴	Exp.	No	NR (NR)	Gym: 12 x 2 x 50 (face-to-face) Home: 12 x 1 45-60	11 and 13 on the RPE	Hospital physio gym (group: home-based)	No	Yes	NR	✓ ✓
51. Mokhtarzade et al. 2017 ⁴⁵	Exp.	No	NR (NR)	8 x 3 x 40-76 (face-to-face)	60% of Max Power	NR	Yes	NR	NR	✓ ✓
52. Mostert et al. 2002 ⁴⁶	Exp.	No	Physician (NR)	3-4 x 5 x 30 (face-to-face)	Aerobic training determined individually by V-slope method during GET	Rehabilitation centre (one to one: NA)	Yes	NR	NR	✓

53. Oken et al. 2004 (1) ⁴⁸	Exp.	No	Physiotherapist (Experience in MS population)	26 x 1 x 60 (face-to-face)	2 – 3 Borg Perceived Exertion Rate	NR (NR: NC)	NR	Yes	NR	✓	✓
54. Petajan et al. 1996 ⁵⁰	Exp.	No	Therapist (NR)	15 x 3 x 50 (face-to-face)	5-minute warm-up at 30% of Vo2max, 30 minutes at 60% of Vo2max	University clinic (NR: NR)	NR	Yes	NR	✓	✓
55. Pilutti et al. 2016 ⁵¹	Exp.	No	Therapist and trainer (NR)	12 x 3 x ≤30 (face-to-face)	RPE: 3 to 4	NR (NR:NC)	Yes	Yes	NR	✓	✓
56. Pompa 2017 ⁵³	Ctrl.		2 x Physiotherapist (NR)	4 x 3 x 20 (face-to-face)	walking exercises on the ground whose difficulty gradually increased	Hospital (individual, none)	Yes	NR	NR	✓	✓
57. Sabapathy et al. 2011 ⁵⁶	Ctrl.	No	Exercise physiologist (NR)	8 x 2 x 55 (face-to-face)	Moderate to hard based on the level of subject's exertion	Community (NR: NC)	Yes	Yes	No	✓	✓
58. Samaei et al. 2016 ⁵⁷	Exp.	No	Qualified therapist (NR)	4 x 3 x 30 (Face-to-face)	55-85% of max HR	NR (individual)	Yes	NR	NR	✓	✓
59. Samaei et al. 2016 ⁵⁷	Ctrl.	No	Qualified therapist (NR)	4 x 3 x 30 (face-to-face)	55-85% of max HR	NR (individual)	Yes	NR	NR	✓	✓
60. Schulz et al. 2004 ⁶⁰	Exp.	No	NR	8 x 2 x 30 (NR)	maximal intensity of 75% of the maximal watts taken from the ergometry results	NR (NR: NA)	Yes	NR	NR	✓	✓
61. Siengsukon et al. 2016 ⁶²	Exp.	No	NR	12 x 3 x 60-70 (NR)	50-59% HR reserve to 60-60% HR reserve	NR (NR: NA)	Yes	NR	NR	✓	✓
62. Skjerbæk et al. 2014 ⁶³	Exp.	No	Physiotherapist (NR)	Total 10 sessions in 4 weeks x 30min (face-to-face)	65%-75% of VO2peak	MS Hospital (one to one and individual: NA)	Yes	Yes	NR	✓	✓

63. Straudi et al. 2014 ⁶⁵	Exp.	No	Physiotherapist (NR)	Clinic: 2 x 5 x 120 (face-to-face); Home: 12 x 3 x 60	Treadmill speed between 0.9 and 2.9 km/h	Outpatient clinic (group: home-based)	Yes	Yes	NR	✓	✓	✓
64. Van den Berg et al. 2006 ⁷²	Exp.	No	Physiotherapist (NR)	4 x 3 x NR (face-to-face)	55– 85% of age predicted maximum HR	NR (one to one: NA)	Yes	Yes	NR	✓		
Resistive												
1. Bulguroglu et al. 2017 (1) ¹⁰	Exp.	No	Physiotherapist (Pilates trainer)	8 x 2 x 60-90 (face-to-face)	Resistance increased with elastic bands	NR (group, NR)	Yes	NR	NR	✓	✓	✓
2. Bulguroglu et al. 2017 (2) ¹⁰	Exp.	No	Physiotherapist (Pilates trainer)	8 x 2 x 60-90 (face-to-face)	Resistance increased with springs	NR (group, NR)	Yes	NR	NR	✓	✓	✓
3. Çakt et al. 2010 (2) ¹¹	Exp.	No	Physical Therapist (NR)	8 x 2 25-30 (unsupervised)	NR	Home based (individual)	No	Yes	NR	✓	✓	
4. Castro-Sanchez et al. 2012 ¹²	Ctrl.	No	Physiotherapist	20 x 2 x 60 (face-to-face)	NR	Therapy room	NR	NR	NR	✓		
5. Collett et al. 2009 (3) ¹³	Exp.	No	Exercise professional (NR)	Research centre: 18 sessions over 12 weeks x 20 (face-to-face) Community/ home: 18 sessions over 12 weeks x 20	20 minutes intermittent cycling at 90% workload	Research centre and community fitness class (individual)	No	Yes	Yes	✓	✓	
6. Dalgas et al. 2010 ¹⁵	Exp.	No	Researcher (NR)	12 x 2 x NR (face-to-face)	NR	NR (group)	Yes	Yes	NR	✓		
7. Dodd et al. 2011 ¹⁷	Exp.	No	Physiotherapist (N/A)	10 x 2 x 45 (face-to-face)	NR	Community (group)	Yes	Yes	NR	✓		
8. Sabapathy et al. 2011 ⁵⁶	Exp.	No	Exercise physiologist (NA)	8 x 2 x 25 (face-to-face)	based on the level of subject's strength and level of progression	Community (NR: NC)	Yes	Yes	No	✓	✓	✓

Balance											
1. Brichetto et al. 2013 ⁷	Exp.	No	NR (NR)	4 x 3 x 60 (face-to-face)	NR	NR (NR)	NR	NR	NR	✓	✓
2. Brichetto et al. 2013 ⁷	Ctrl.	No	NR (NR)	4 x 3 x 60 (face-to-face)	NR	NR (NR)	NR	NR	NR	✓	✓
3. Brichetto et al. 2015 ⁸	Exp.	No	Therapist (NR)	4 x 3 x 60 (NR)	NR	NR (NR)	Yes	NR	NR	✓	✓
4. Brichetto et al. 2015 ⁸	Ctrl.	No	Therapist (NR)	4 x 4 x 60	NR	NR	Yes	NR	NR	✓	✓
5. Frevel et al. 2015 ²¹	Exp.	No	Exercise therapist (N/A)	12 x 2 x 45 (web-based)	Moderate intensity	Home-based (individual)	Yes	NR	NR	✓	✓
6. Frevel et al. 2015 ²¹	Ctrl.	No	Horse riding therapist	12 x 2 x 30 (face-to-face)	NR	Riding centre (one to one)	Yes	NR	NR	✓	✓
7. Gandolfi et al. 2014 ²²	Exp.	Yes	Physiotherapist	12 x 2 x 50 (face-to-face)	NR	NR (one to one)	Yes	NR	NR		✓
8. Gandolfi et al. 2014 ²²	Ctrl.	Yes	Physiotherapist	12 x 2 x 50 (face-to-face)	NR	NR	Yes	NR	NR		✓
9. Gandolfi et al. 2015 ²³	Exp.	No	Physical Therapist (treatment protocol)	5 x 3 50 (face-to-face)	N/A	Neurological Rehabilitation (one to one)	Yes	Yes	Yes		✓
10. Hebert et al. 2011 (1) ²⁸	Exp.	No	1 x Physical therapist (12 yrs experience in treating MS patients)	(a) 6 x 2 x 55 (Face-to-face) (b) 10 x 7 x 40 (Home-based)	N/A	(a) Research Centre (NR: NR) (b) Home-based (individual: NA)	No	Yes	NR		✓
11. Hebert et al. 2018 ²⁹	Exp.	Yes	NR	Phase 1: 6 x 2 x 60 (face-to-face, home) Phase 2: 8 x 1 x 60 (face-to-face, home)	N/A	Home-based (individual: NR)	Yes	Yes	NR		✓
12. Pilutti et al. 2016 ⁵¹	Ctrl.	No	Trainer	12 x 3 x 30 (face-to-face)	NR	NR	Yes	Yes	NR	✓	✓
13. Vermohlen et al. 2018 ⁷⁵	Exp.	No	As per German hippotherapy regulations	12 x 1 (face-to-face)	NR	Hippotherapy centre (NR:NR)	NR	NR	NR		✓

Flexibility

1. Hugos et al. 2017 ³²	Exp.	No	Physiotherapist (with assistance from study coordinator)	4 x 2 classes only x 120 (face-to-face) Home: booklet, DVD and exercise diary	N/A	Research centre + home-based (group + individual)	NR	NR	NR	✓	✓
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Combined

1. Alguacil Diego et al. 2012 ²	Exp.	Yes	NR (NR)	1 x 5 x 10 (NR)	1min duration at 6Hz frequency with amplitudes below 4mm (A=3mm) with 1minutes pause in between	Research centre (NR)	Yes	NR	NR	✓	✓
2. Aydin et al. 2012 ⁴	Exp.	No	Physiatrist (N/A)	12 x 3 x 60 (face-to-face)	NR	University hospital (NR)	No	NR	NR	✓	✓
3. Aydin et al. 2012 ⁴	Ctrl.	No	NR	12 x 5 x 60	NR	Home-based (Individual: yes)	NR	NR	NR	✓	✓
4. Bansi et al. 2012 ⁶	Exp.	Yes	Physiotherapist (N/A)	NR (face-to-face)	70% of HR max or 60% VO2 max	Rehabilitation centre (NR)	Yes	NR	NR	✓	✓
5. Çakta et al. 2010 (1) ¹¹	Exp.	No	Physical Therapist (NR)	8 x 2 115-130 (face-to-face)	2 min of high resistance ergometer (40% of tolerated maximum weight) followed by 2 min of low resistance (30-40 W) pedalling	NR (group)	Yes	Yes	NR	✓	✓
6. Collett et al. 2009 (2) ¹³	Exp.	No	Exercise professional (NR)	Research centre: 18 sessions over 12 weeks x 20 (face-to-face) Community/ home: 18 sessions over 12 weeks x 20	10 Minutes continuous cycling at 45% workload + 10 minutes intermittent cycling at 90% workload	Research centre and community fitness class (one to one and individual)	No	Yes	Yes	✓	✓

7. Coote et al. 2017 ¹⁴	Exp.	No	Physiotherapist (trained to deliver program)	6 group sessions (face-to-face) 14 home strengthening, 20 home walking and 4 telephone calls over 10 weeks	walking programme 100 steps a minute at increasing duration: strength 10-15 reps at intensity that they would fail at 12 th rep	Community centres (group) Home sessions	Yes	Yes	Yes	✓	✓
8. Coote et al. 2017 ¹⁴	Ctrl.	No	Physiotherapist (trained to deliver program)	6 group sessions (face-to-face) 14 home strengthening, 20 home walking and 4 telephone calls over 10 weeks	walking programme 100 steps a minute at increasing duration: strength 10-15 reps at intensity that they would fail at 12 th rep	Community centres (group) Home sessions	Yes	Yes	Yes	✓	✓
9. Ebrahimi et al. 2015 ¹⁸	Exp.	Yes	NR	10 x 3 x NR (face-to-face)	WBV (frequency and amplitude were set at 2-20 Hz and 2 mm, respectively) consisted of 15 sets of vibrations with three repetitions	NR (NR)	Yes	NR	NR	✓	✓
10. Escudero-Uribe et al. 2017(1) ¹⁹	Exp.	Yes	Neurologic physical therapist	12 x 2 x 60-100 (face-to-face)	WBV (frequency and amplitude were set at 4Hz ±1Hz/sec and 3mm respectively) RPE from 11-15	NR (group)	Yes	Yes	NR	✓	✓
11. Escudero-Uribe et al. 2017(2) ¹⁹	Exp.	Yes	Neurologic physical therapist	12 x 2 x 60-100 (face-to-face)	BT RPE from 11-15	NR (group)	Yes	Yes	NR	✓	✓
12. Gandolfi et al. 2015 ²³	Ctrl.	No	Physical therapist	5 x 3 x 50 (face-to-face)	NR	Rehabilitation unit (NR:NR)	Yes	Yes	Yes	✓	✓

13. Garrett et al. 2012 (1) ²⁴	Exp.	No	Physiotherapist (manual)	Aerobic: 10 x 2 x 30 + 10 x 3 30 Resistive: 10 x 1 x 60 + 10 x 2 x 60 (NR)	Aerobic: 65% heart rate max Resistive: 3 sets with failing on the 12th repetition of the exercise	Community (group)	Yes	Yes	Yes	✓	✓
14. Garrett et al. 2012 (2) ²⁴	Exp.	No	Fitness instructor (NC)	10 x 1 x 60 (face-to-face)	NC	Community (group)	NR	NR	NR	✓	✓
15. Hayes et al. 2011 ²⁷	Exp.	No	NR	12 x 3 x 45-60 (face-to-face + instructional)	Started at 7/20 and progresses to 13/20 on Borg Scale + increase load each session	NR (NR; NR)	NR	Yes	NR	✓	✓
16. Hogan et al. 2014 (1) ³¹	Exp.	No	Physiotherapist (Manual, and instruction)	10 x 1 x 60 (face-to-face)	Progressed depending on the ability of participants	Community (group: NA)	Yes	Yes	NR	✓	✓
17. Kerling et al. 2015 ³⁷	Exp.	No	Sport scientist (NR)	12 x 2 x 40 (face-to-face)	Resistive: 13 on the RPE Aerobic: 50% max workload	Institute of Sports Sciences (NR)	Yes	NR	NR	✓	✓
18. Kern 2013 ³⁸	Exp.	No	2 x Physiotherapist 2 x experienced climbers	22 x 1 x 120 (1 st 2 weeks) 60 (remaining) (face-to-face)	Progressed depending on the ability of participants	Community (group: NA)	No	Yes	No	✓	✓
19. Learmonth et al. 2011 ⁴¹	Exp.	No	Physiotherapist & Fitness instructor (NR)	12 x 2 x 60 (face-to-face)	Decided by participant through discussion with instructor	Community (group: NA)	Yes	Yes	NR	✓	✓
20. Learmonth et al. 2017 ⁴²	Exp.	No	NR	Aerobic: 16 x 2 x 10- 30 Strength: 16 x 2 (Web-based) SCT: 6 newsletters + 8 video sessions	Moderate intensity	Home-based (individual)	Yes	Yes	NR	✓	✓

21. Ozkul et al. 2018 ⁴⁹	Exp.	No	Physiotherapist (NR)	Aerobic: 8 x 3 x 30 Pilates: 8 x 3 x 60 (face-to-face)	Aerobic: 60-80% of MHR Pilates: 10-20 repetitions each exercise	University clinic (NR:NR)	Yes	Yes	NR	✓	✓	✓	✓
22. Pompa et al. 2017 ⁵³	Exp.	No	2 x Physiotherapists (NR)	4 x 3 x 20 (face-to-face)	40%-50% of patients' body weight, between 1.3-1.8 km/h	Hospital (individual, none)	Yes	NR	NR	✓	✓	✓	✓
23. Romberg et al. 2005 ⁵⁵	Exp.	No	Physiotherapist (NR)	Rehabilitation centre: 26 x 10 x NC (face-to-face); Home: 4-26 x 3-4 x NC	NR	Neurological Rehabilitation Centre (group: home exercise)	No	Yes	NR	✓	✓		
24. Sangelaji et al. 2014 ⁵⁹	Exp.	No	Therapist (NR)	10 x 3 x 90 (face-to-face)	Aerobic: 40 – 70% Max HR; timing increased each session	MS therapy centre (NR: NA)	Yes	No	NR	✓	✓	✓	✓
25. Tallner et al. 2013 ⁶⁷	Exp.	No	Therapist (NR)	24 x 3 20±15.4 (Web based)	6 to 20 BORG Scale	Home-based (individual)	Yes	Yes	NR	✓	✓		
26. Tallner et al. 2016 ⁶⁸	Exp.	No	Exercise/Physical therapists (NR)	Strength training: 12 x 2 Endurance training: 12 x 1 (Web based)	11 to 16 BORG Scale	Home-based (individual)	Yes	Yes	NR	✓	✓		
27. Tarakci et al. 2013 ⁶⁹	Exp.	No	Physical therapist (NR)	12 x 3 x 60 (face-to-face)	Rest at 13/20 RPE	Hospital rehabilitation unit (Group: NA)	Yes	No	No	✓	✓	✓	
28. Uszynski et al. 2014 ⁷⁰	Exp.	No	Physiotherapist (NR)	8 x 3 x 20-30 (33% face-to-face + 66% unsupervised)	NR, but intensity increased depending on individual need	Community (NR; NA)	Yes	Yes	No	✓	✓		
29. Uszynski et al. 2014 ⁷⁰	Ctrl.	No	Physiotherapist - 1 session a week (NR)	8 x 3 x 30 (face-to-face)	Subjects rated Borgs scale	NR	Yes	Yes	NR	✓			
30. Uszynski et al. 2015 ⁷¹	Exp.	No	Physiotherapist and Physiotherapist assistant (NR)	12 x 3 x NR (face-to-face)	NR	Outpatient MS centre (group; NA)	Yes	Yes	No	✓	✓		
31. Uszynski et al. 2015 ⁷¹	Ctrl.	No	Physiotherapist (NR)	12 x 3	NR	MS therapy centre (NR: NR)	Yes	Yes	NR	✓			

32. Velikonja et al. 2010 ⁷⁴	Exp.	No	Sports Climbing Instructor x 2 (Licenced)	10 x 1 x NR (face-to-face)	NR	Training, Occupation and Care Centre (Face-to-face: NA)	Yes	No	No	✓	✓	✓
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Abbreviations: Ctrl (Control group); Exp (Experimental group); HR (heart rate); NA (Not applicable); NC (Not clear from text); NR (Not reported).

Supplementary Table B3: Template for intervention Description and Replication (TiDiER) characteristics for behavioural and combined treatments (emboldened studies were significantly effective at post-treatment in pairwise meta-analyses)

Study reference	Exp. / Ctrl.	Theory/ rationale	Who delivered (level of training)	Timing & Mode of Delivery (week x frequency x minutes (mode))	Setting (format: homework)	Tailoring	Adherence Assessed	Fidelity Assessed
Behavioural techniques with PA								
1. Bombardier et al. 2008 ¹²⁰	Exp.	NR	1 x Research care manager (attended 2-day training on MI, received additional training)	1 x 90 (face-to-face session) 12 x 5 (biweekly) x 30 (tel)	MS centre and Home-based (individual: yes)	No	Yes	Yes
2. Carter et al. 2014 ¹²¹	Exp.	NR	Physiotherapist	6 x 2 x 60 + 6 x 1 x 60 (face-to-face) Exercise: 6 x 1 x 60 + 6 x 2 x 60 (home), 50%–69% of predicted maximum heart rate (220-age) or 12–14 on the Borg Ratings of Perceived Exertion Scale	Research centre + community + home-based (group + individual)	Yes	Yes	NR
3. Ennis et al. 2006 ¹²⁴	Exp.	NR: Self-efficacy is reported to influence health-promoting behaviour, the practical sessions aim was to give participants knowledge to make informed decisions, and provide opportunities to experience successful performance, in a safe and supportive environment.	NR x Occupational therapist, physiotherapist, dietician and MS specialist nurse (NR)	8 x 1 x 180 (face-to-face)	Hospital facility (group; NR)	NC	Yes	NR
4. O'Hara et al. 2002 ¹³⁰	Exp.	NR	NR	4 x 2 x 120 (face-to-face and booklet)	Home-based and local therapy centres ((a) group or (b) individual: NR)	NR	NR	No
5. Pilutti et al. 2014 ¹³³	Exp.	NC: Principles of Social Cognitive Theory.	3 x behavioural coaches (highly trained doctoral students or a postdoctoral fellow; followed principles of supportive accountability in TeleCoach guidelines)	24 x 15 sessions (frequency NR) x NR (web/face-to-face video)	Home-based (individual: NR)	NC	NR	NR
6. Plow et al. 2009 ⁵²	Ctrl.	EC principles with empirical support from previous studies.	NR x Therapist (NR)	7 x 1 x 120 (face-to-face) and extra 2 x NR for pwMS who missed sessions (tel)	Clinic and Home-based (individual: NA)	Yes	Yes	NR

7. Smith et al. 2012 ⁶⁴	Ctrl.	NR: Cites evidence in support of MI to facilitate adherence to exercise and affect in response to exercise.	Physiotherapist (NR)	8x3x (15-60) (face-to-face)	NR (group, NR)	NR	Yes	NR
8. Stuijbergen et al. 2003 ¹³⁵	Exp.	A conceptual model integrating elements from the health belief model, Pender model of health promotion, and self-efficacy theory. Authors suggest an intervention designed to focus on the development of knowledge and skills will reduce barriers and enhance resources and self-efficacy, resulting in greater participation in health-promoting behaviours and greater QoL.	NR x Nurse (NR)	Cohort 1 and 2: 8 x 1 x 90 (face-to-face) 12 x 2 every 4 weeks x NR (follow-up tel) Cohorts 3, 4 and 5: 8 x fortnightly x 180 12 x 2 every 4 weeks x NR (follow-up tel)	Community (NR; NR)	Yes	Yes	NR
9. Thomas et al. 2017 ¹³⁶	Exp.	NR: Cites evidence for the benefits of exercise in MS and the practical advantages of Wii and the importance of behavioural strategies to support behaviour change.	2 x Physiotherapists (trained to Mii-vitaliSe)	24 x 1 (face-to-face)	Hospital: (face-to-face) Home-based: (individual)	Yes	Yes	NR
Cognitive behavioural therapy for fatigue								
High intensity therapy								
1. van den Akker et al. 2017 ¹¹⁷	Exp.	Empirically validated cognitive behavioural model of MS fatigue	6 x CBT Therapists / State Healthcare Psychologists	Over 16 weeks 12 x 45 (face-to-face) (previously CBT trained; 3-day training)	Outpatient Clinic (individual: Yes)	Yes	Yes	NR
2. van Kessel et al. 2008 ¹¹⁸	Exp.	Empirically validated cognitive behavioural model of MS fatigue	1 x Clinical Psychologist (previously CBT trained)	Over 8 weeks 3 x 50 (face-to-face) Over 8 weeks 5 x 50 (tel)	Hospital facility (individual: Yes)	Yes	Yes	Yes
Cognitive behavioural therapy for fatigue								
Low intensity therapy								
1. Moss-Morris et al. 2012 ¹⁰³	Exp.	Empirically validated cognitive behavioural model of MS fatigue	1 x Assistant Psychologist (5 hours basic training in interventions)	8 x 1 x 50 (web) Over 8 weeks 3 x 60 (tel)	Home-based (individual: Yes)	Yes	Yes	Yes
2. Pöttgen et al. 2018 ¹⁰⁶	Exp.	Empirically validated cognitive behavioural model of MS fatigue	Developed by a Clinical Psychologist (NR)	8 x 1 x 60 (web)	Home-based (individual: Yes)	Yes	Yes	NA
3. van Kessel et al. 2015 ¹¹⁹	Exp.	Empirically validated cognitive behavioural model of MS fatigue	1 x Clinical Psychologist	8 x 1 x 10 (email) 8 x 1 x 50 (web)	Home-based (individual: Yes)	Yes	Yes	NA

(previously CBT trained)								
Cognitive behavioural therapy for distress-related outcomes								
Self-help alone								
1. Fischer et al. 2015 ⁸⁶	Exp.	Several approaches: behavioural activation and cognitive modification, mindfulness and acceptance, interpersonal skills, relaxation, physical exercise and lifestyle modification, problem solving, childhood experiences and early schemas, positive psychology interventions, dream work and emotion-focused interventions and psychoeducation.	NA	9 x 1 x 60 (web)	Home-based (individual: yes)	Yes	Yes	NA
Cognitive behavioural therapy for distress-related outcomes								
High intensity therapy								
1. Alisaleh & Shahrbano 2016 ⁷⁶	Exp.	NR: MBSR. Suggests main mechanism is controlling attention and cites other MBCT for fatigue and anxiety in MS.	NR	8 x 1 x 120-150 (face-to-face)	NR (group: yes)	No	NR	NR
2. Bogosian et al. 2015 ⁷⁹	Exp.	NR; MBCT. Cites evidence for mindfulness training in supporting adjustment in other illness and MS samples, but not specifically for SPMS.	1 x Health Psychologist (completed a recognized mindfulness teacher training course)	8 x 1 x 60 (Skype®)	Home-based (group: yes)	Yes	NR	Yes
3. Carletto et al. 2017 ⁸⁰	Exp.	NC: Cites evidence for mindfulness training in supporting adjustment in other illness and MS samples. Suggests that mindfulness can lead patients to relate to their physical and psychological symptoms in a different way, with a positive effect on coping strategies and adaptation to the disease.	NR x Psychologists	1 x 8 x 180 (psychologist face-to-face); plus, all-day 420 session	Hospital facility (group: yes)	Yes	NR	NR
4. Cavalera et al. 2018 ⁸¹	Exp.	NC: Online MBSR	Research team (NR)	8 x 1 x NC (videoconferencing)	On-line delivery (group: yes)	NR	NR	NR
5. Graziano et al. 2013 ⁹¹	Exp.	NC: CBT for depression and adjustment to MS: Cites review evidence for efficacy of CBT as applied to pwMS.	1 x psychologist (experience of running groups based on CBT principles)	8 x 2 biweekly x 120 (face-to-face)	Community (group: yes)	Yes	Yes	No
6. Grossman et al. 2010 ⁹²	Exp.	NR: MBSR.	1 x Experienced certified teacher (>9 years of experience)	8 x 1 x 180 (face-to-face)	Hospital facility and university (group: yes)	No	Yes	NR

7. Kiropoulos et al. 2016 ⁹⁴	Exp.	CBT based on Beck's cognitive theoretical model for the treatment of depression in adults.	1 x Senior clinical psychologist 1 x Provisional clinical psychologist	8 x 1 x 60 (session 1 was 90) (face-to-face)	Hospital facility (individual: yes)	Yes	Yes	No
8. Mohr et al. 2003 (1) ⁹⁴	Exp.	Standard CBT: cites studies showing associations between negative affect and physical symptom reporting in other populations, and depressed mood postdoctoral clinical experience is associated with increases in self-reported severity fatigue. PwMS with high negative affect may be more likely to attend to or complain about physical symptoms.	4 x CBT therapists / psychologists (range of 1-8 years of postdoctoral clinical experience)	16 x 1 x 50 (face-to-face)	NR (individual: yes)	Yes	NR	Yes
9. Simpson et al., 2017 ¹¹¹	Exp.	NC: Refers definitions of mindfulness and cites evidence in the context of chronic pain and other long-term health conditions.	2 x experienced physician facilitators with training in MBSR and MBCT)	8 x 1 x NR (face-to-face)	Hospital facility (group: yes)	Yes	Yes	Yes
Education								
1. Carletto et al. 2017 ⁸⁰	Ctrl.	NR: Based on a psycho-educational framework and involved discussion of MS-related topics. The group practiced relaxation techniques and gentle stretching exercises at the end of each session. This was to control for non-specific treatment factors.	1 x psychotherapist with experience in relaxation training and in working with people with MS	1 x 8 x 180 (psychologist face-to-face)	Hospital facility (group: yes)	NC	NR	NR
2. Cavalera et al. 2018 ⁸¹	Ctrl.	On-line psychoeducation dealing with stress management, relaxation, sleep hygiene, fatigue, and social relationships.	NR	8 x 1 x NR (videoconferencing)	On-line (NR: Yes)	Yes	NR	NR
3. Ehde et al. 2015 ⁸³	Ctrl.	NC: Telephone delivered education on MS symptoms and care	Therapist (2 masters level social workers, 2 doctoral level psychologists, experienced psychologist)	8 x 8 x 60 (tel) 2 x 2 x 15 (follow-up tel)	Home-based (individual; NR)	Yes	Yes	Yes
4. Ghahari et al. 2010 (2) information only ⁹⁰	Exp.	EC principles with empirical support from previous studies	1 x experienced neurological occupational therapist	6 x 1 x 180 (web)	Home-based (individual: Yes)	NC	NR	NR

5. Garcia Jalon et al. 2012 ⁸⁹	Ctrl.	NR: Peer support consisting of education and discussion of common topics for pwMS as recommended by the MS Society, the MS Trust and Action MS to control for non-specific treatment factors.	1 x Physiotherapist (not clear)	5 x 1 x 120 (face-to-face)	Community (group: Yes but content unclear)	Yes	NR	NR
6. Graziano et al. 2013 ⁹¹	Ctrl.	NR: Informative sessions about stem cells, complementary and alternative therapies, and nourishment.	Different therapists (NR)	3 sessions	Community (group: yes)	No	NR	NR
7. Hugos et al. 2018/2019 ^{127, 128}	Ctrl.	NR: Used educational pamphlets from the National MS Society	1 x Different MS professionals with at least one year of experience NC	6 x 1 x 120 (face-to-face: manual and DVD) 4 x 1 x 120 (face-to-face)	Academic medical centre MS clinics (group: yes) NR (group: No)	Yes	Yes	Yes
8. Kos et al. 2007 ⁹⁵	Ctrl.	NR: Interesting topics chosen to minimize attrition, but not directly related to fatigue, such as car adaptations and driving abilities, communication skills, lift techniques for back protection and general information about MS.				NC	NR	NR
9. Mackay et al. 2015 ⁹⁷	Ctrl.	NC: Relaxation, mindfulness, social support and education.	Therapist (NR)	5 x 3 x 60 (face- to-face)	Hospital sites (individual, NA)	NR	NR	NR
10. Rietberg et al. 2014 ¹³²	Ctrl.	NR: Consultation according to the Nursing Intervention Classification. Goals were set during a one-hour session, and subsequently evaluated in follow-up consultations every three weeks. The nurse discussed general principles of planning of activities, priority setting, energy conservation, accepting help from others with daily life activities or use of devices. Physical activity was recommended. Patients were advised on nutrition and alcohol and drug intake. In addition to the consultation sessions, the patients were given homework assignments.	Nurse (NC)	1x60 (face-to-face), follow-up consultations every 3 weeks (NC)	Outpatient Clinic (group/individual: Yes)	Yes	Yes	NR

11. Turner et al. 2016 ¹³⁷	Ctrl.	NR: Used home DVD designed by the US Department of Veterans Affairs to promote physical activity. This educational program provided health information to facilitate motivation, provided age, gender and ability-matched peer models to promote self-efficacy, and provided numerous examples of practical and sustainable in-home exercises to overcome barriers to participation. This control group was selected to separate potential benefits of telephone counselling and home monitoring from physical activity education alone.	NA	NA	Home-based (individual: NA)	No	NR	NA
12. van Kessel et al. 2015 ¹¹⁹	Ctrl.	Empirically validated cognitive behavioural model of MS fatigue	NA	NA	Home-based (individual: Yes)	Yes	Yes	NA
Energy conservation with elements of CBT								
1. Ehde et al. 2015 ⁸³	Exp.	NC: CBT for symptom management, cites evidence supporting effectiveness of self-management interventions developed from other evidence-based cognitive-behavioural and educational interventions.	2 x Social workers 2 x Psychologists (received training and supervision from the PI: psychologist with >20 years of expertise in the study population and interventions)	8 x 1 x 60 (tel)	Home-based (individual: yes)	Yes	Yes	Yes
2. Mohr et al. 2007 ¹⁰²	Exp.	NR: CBT for depression. Cites evidence for telephone-based CBT being effective at reducing depression and improving positive affect in other populations, including MS.	5 x CBT therapists / psychologist (range of 1-5 years of postdoctoral clinical experience; 2 days of training and conducted 12 weeks of supervised therapy with 2 practice patients; received 2 hours of weekly group supervision by a senior psychologist)	16 x 1 x 50 (tel)	Home-based (individual: NR)	Yes	NR	Yes
3. Thomas et al. 2013 / 2014 ^{115, 116}	Exp.	CBT, energy effectiveness (incorporates some EC principles) and social cognitive theory	8 x health care professionals (Occupational Therapists, Physiotherapists, MS Nurse) in 3 centres (1-day workshop training in delivery of intervention)	Over 6 weeks 1 x 120, 5 x 105 (face-to-face)	Community (hotels) & rehabilitation hospital (group: Yes)	Yes	Yes	No
Energy conservation								

1. Blikman et al. 2017 ⁷⁸	Exp.	EC principles with empirical support from previous studies and some MI	5 x Occupational therapist (programme guideline and 1 day refresher course; qualified in MI)	Over 16 weeks 12 x 45 (face-to-face and workbook)	Outpatient Clinic (Individual: Yes)	Yes	Yes	Yes
2. Eyssen et al. 2013 ⁸⁴	Exp.	EC principles with empirical support from previous studies and cites importance of client-centred care.	NR x Occupational Therapists (OTs received a two-day course in client-centred practice and four booster sessions)	32 x 1 every month x 420 (face-to-face)	Hospital facility or rehabilitation centre as multi-site study (individual: NR)	Yes	No	Yes
3. Finlayson et al. 2011 ⁸⁵	Exp.	EC principles with empirical support from previous studies	1 x Occupational therapist (pre-training by PI)	6 x 1 x 70 (tel)	Home-based (group: Yes)	Yes	NR	NR
4. Ghahari et al. 2010 (1) information and interactive elements ⁹⁰	Exp.	EC principles with empirical support from previous studies	NR x Occupational therapist specialists in neurological conditions (2 days training)	6 x 1 x 180 (web)	Home-based (individual: Yes)	NC	NR	NR
5. Garcia-Burguillo Aguila-Maturana 2009 ⁸⁸	Exp.	EC principles with empirical support from previous studies	NR	10 x 2 x 120 (face-to-face)	NR (group: NR)	NC	Yes	NR
6. Garcia Jalon et al. 2012 ⁸⁹	Exp.	EC principles with empirical support from previous studies	1 x Physiotherapist (not clear)	5 x 1 x 120 (face-to-face)	Community (group: Yes but content unclear)	Yes	NR	NR
7. Kos et al. 2007 ⁹⁵	Exp.	EC principles with empirical support from previous studies	1 x Doctor, Psychologist, Physiotherapist and Occupational Therapist (per session) (not clear)	4 x 1 x 120 (face-to-face)	NR (group: No)	Yes	NR	NR
8. Kos et al. 2016 ⁹⁶	Exp.	EC principles with empirical support from previous studies & some MI	1 x experienced Occupational Therapist	3 x 1 x 60-90 (face-to-face with booklet)	NR (Individual: Yes)	Yes	NR	NR
9. Mathiowetz et al. 2005/2007 ^{98, 99}	Exp.	EC principles and self-efficacy theory generally	12 x Certified occupational therapists (1-hour training session for all therapists)	6 x 1 x 120 (face-to-face)	Community (group: Yes)	Yes	Yes	Yes

Energy conservation and aerobic exercise

1. Hugos et al. 2010 ¹²⁶	Exp.	EC principles with empirical support from previous studies	1 x Physical therapist (Informal introduction by PI)	6 x 1 x 120 (face-to-face: Manual and DVD) Exercise: 6 x 1 x 20 to 30 (face-to-face: Manual and DVD), 3-5 of RPE	Community (group: Yes)	Yes	Yes	NR
2. Hugos et al. 2018/2019 ^{127, 128}	Exp.	EC principles with empirical support from previous studies	1 x Different MS professionals with at least one year of experience	6 x 1 x 120 (face-to-face: Manual and DVD)	Academic medical centre MS clinics (group: yes)	Yes	Yes	Yes
3. Rietberg et al. 2014 ¹³²	Exp.	EC principles with empirical support from previous studies	NR x Physical therapist or Occupational therapist or Social worker (none)	12 x 2 x 45 (face-to-face) Exercise intensity: 50 – 70 % VO2 peak	Outpatient Clinic (group/individual: Yes)	Yes	Yes	NR
Emotional expression therapy								
1. Mohr et al. 2003 (2) ¹⁰¹	Exp.	NR: Supportive expressive group therapy originally developed and validated on research with women with breast cancer. Incorporated interpersonal group processes described by Irvine Yalom (1995).	5 x Supportive expressive group therapists / psychologists (1-9 years of postdoctoral clinical experience)	16 x 1 x 90 (face-to-face)	NR (group: yes)	Yes	NR	Yes
2. Mohr et al. 2007 ¹⁰²	Exp.	NC: Telephone-administered supportive emotion-focused therapy is an adaptation of the manual developed by Greenberg et al. (1993) for process experiential psychotherapy.	Psychologist (2 days training and conducted 12 weeks of supervised therapy with 2 patients. 1-9 years of postdoctoral clinical experience)	16 x 1 x 50 (telephone calls)	Homebased (individual, NR)	No	NR	Yes
3. Sterz et al. 2013 ¹¹²	Exp.	NC: Based on the principle: activate resources, increase responsibility an interactive self-management program for young and newly diagnosed people with MS.	NR	3 to 8 (varied) x 2 x 60 (face-to-face)	NR (group: yes)	NR	NR	NR
Combined Motivational Interviewing and Physical Activity Promotion								
1. Turner et al. 2016 ¹³⁷	Exp.	EC and MI principles	1 x Therapist (Multiday MI training program conducted by an experienced MI trainer)	6 x 1 x 41.8 (tel)	Home-based (individual: Yes)	Yes	Yes	Yes

Exercise: 6 x 1-7 x 15-45 (DVD and booklet), moderate intensity								
Neurocognitive rehabilitation								
1. Amato et al. 2014 ⁷⁷	Exp.	NR: Cite some preliminary evidence to suggest that individual computer-assisted cognitive rehabilitation can result in improved performance.	1 x Neuropsychologist	1 x duration NR (initial face-to-face training session) 12 x 2 x 60 (computer-training sessions)	Home-based (group: yes)	No	NR	Yes
2. Amato et al. 2014 ⁷⁷	Ctrl.	NR: Cite some preliminary evidence to suggest that individual computer-assisted cognitive rehabilitation can result in improved performance.	1 x Neuropsychologist	1 x duration NR (initial face-to-face training session) 12 x 2 x 60 (computer-training sessions)	Home-based (group: yes)	No	NR	Yes
3. Choobforoushzadeh et al. 2015 ⁸²	Exp.	NC: Biofeedback. Cites evidence for biological mechanisms of depression related to differential activation between the right and left prefrontal cortices.	NR	8 x 2 x 32 (NR)	Hospital facility (group: yes)	NR	NR	NR
4. Flachenecker et. al. 2017 ⁸⁷	Exp.	NC: Attentional deficit could be associated with MS fatigue.	1 x Neuropsychologist	2 x 5 x (2x30) (face to face)	NC (computer-based: no)	Yes	NR	NR
5. Flachenecker et al. 2017 ⁸⁷	Ctrl.	NC: Attentional deficit could be associated with MS fatigue.	1 x Neuropsychologist	2 x 5 x (2x30) (face to face)	NC (computer-based: no)	Yes	NR	NR
6. Grasso et al. 2017 ¹²⁵	Exp.	NC: Based on the Attention Processing Training program for sustained, selective, alternating, and divided attention.	1 x Cognitive Rehabilitation Specialist	12 x 3 x NR (NR)	NC (individual: yes)	No	NR	NR
7. Hildebrandt et al. 2007 ⁹³	Exp.	NC: Cites previous evidence for neurocognitive interventions improving visual perception and memory performance and word generation.	NA	6 x 5 days per week x 30 (CD computer-based training)	Home-based (individual: NA)	No	NR	NA

8. Mattioli et al. 2015 ¹⁰⁰	Exp.	NC: Cites previous research in improving trained function in cognitive domains.	1 x Neuropsychologist (Expert)	13 x 60 x 60 (computer-based training)	Home-based and hospital facility (individual: NA)	Yes	NR	NR
9. Pérez-Martín et al. 2017 ¹⁰⁵	Exp.	NC: Cites evidence for individual computer-assisted cognitive rehabilitation programmes that improve performance on neuropsychological tests.	NR	12 x 1 x 75 (computer and booklet training)	Hospital facility (individual: yes)	No	Yes	NR
10. Rosti-Otajärvi et al. 2013 ¹⁰⁷	Exp.	NC: Cites evidence for cognitive retraining combined with neuropsychological counselling and teaching compensatory strategies improves cognitive performance, reduces depressive and fatigue symptoms	1 x Neuropsychologist (NR)	13 x 1 x 60 (face-to-face with computer-based training)	Home-based (individual: NA)	Yes	Yes	NR
11. Tesar et al. 2005 ¹¹⁴	Exp.	NR	NR	4 x 4 x 90 (face-to-face with computer-based training)	Outpatient facility (individual: NR)	No	NR	NR
Physical rehabilitation programmes (occupational therapy and physiotherapy)								
1. Craig et al. 2003 ¹²²	Exp.	NR: Cites evidence for the benefits of physiotherapy and occupational therapy.	NR (whole services) x Physiotherapists and Occupational Therapists (NR)	NR	NR (NR; NR)	Yes	Yes	NR
2. Di Fabio et al. 1998 ¹²³	Exp.	NR	NR x Physiotherapists and Occupational Therapists (NR)	52 x 1 x 300 (face-to-face)	MS centre (NR; NR)	Yes	No	No
3. Grasso et al. 2017 ¹²⁵	Ctrl.	NR	Physiotherapist and Occupational Therapist (NR)	10 x 10 x 45 (face to face)	N/A	Yes	NR	NR
4. Patti et al. 2002 ¹³¹	Exp.	NR: Cites evidence for physical rehabilitation programmes.	NR x Physiotherapists, Occupational Therapists and Neurologists (NR)	6 x (6 per week) x NR (face-to-face)	NR (group and individual: yes)	Yes	NR	NR
5. Storr et al. 2006 ¹³⁴	Exp.	NR	NR x Physiotherapists, Occupational Therapists, Psychologists, Social Workers, Nurses and Neurologists (NR)	5 x 5 times weekly x 45 (physio face-to-face) 5 x 3 times weekly x 30 (occupational therapy face-to-face)	MS rehabilitation hospital (individual: NA)	Yes	NR	NR

Combined Multidisciplinary rehabilitation program (incl. aerobic exercise) with high-dose methylprednisolone								
1. Nedeljkovic et al. 2016 ¹²⁹	Exp.	No	Neurologist, rehabilitation physician, social worker, physiotherapist, occupational therapist and nurse (NR)	PT: 3 x 5 x 60 (face-to-face) OT: 3 x 3 x 30 (NR) Counselling: 2 times x 30 min (face-to-face) Gradual increase of level of exercise	Neurology clinic and home-based (individual: NR)	Yes	NR	NR
Relaxation and biofeedback								
Relaxation and biofeedback								
1. Carletto et al. 2017 ⁸⁰	Ctrl.	NC: Discussion on MS-related topics, relaxation practice. No evidence cited.	NR x Psychologist	1 x 8 x 180 (psychologist face-to-face)	Hospital facility (group: yes)	Yes	NR	NR
2. Kos et al. 2016 ⁹⁶	Ctrl.	NR: Relaxation program included education on the role of stress (management) in MS and practicing relaxation techniques such as Jacobson, Schultz, visualization.	1 x experienced Physical Therapist	3 x 1 x 60-90 (face-to-face with booklet)	NR (Individual: Yes)	Yes	NR	NR
3. Mackay et al. 2015 ⁹⁷	Exp.	NC: Relaxation, mindfulness, social support, and education with biofeedback Suggests psychosocial interventions place too greater emphasis on therapist contact rather than enhancing internal locus of control / self-regulatory processes. Cites evidence in chronic pain for biofeedback, which focuses more on self-regulation.	1 x Psychologist (experience of running biofeedback sessions in neurology clinics)	3 x 3 x 60 (face-to-face)	Three Hospital facilities (individual: yes)	NR	NR	NR
4. Nazari et al. 2015 ¹⁰⁴	Exp.	NR - no empirical support in MS described	NR	4 x 2 x 40 (face-to-face)	NR	NR	NR	NR
5. Seebacher et al. 2015 (1) and (2) ¹⁰⁸	Exp.	Suggests sensorimotor synchronisation to rhythmic auditory stimuli may impact on motor imagery. Listening to music is also hypothesised to be beneficial in terms of enhancing motivation improving mood and productivity, and in turn walking performance and imagined walking.	1 x Experienced physiotherapist (NR)	NR 4 x 6 x 17 (Motor imagery CD and practice) 4 x 1 x NR (tel)	Home-based and introductory session (location NR) (individual: NA)	NR	Yes	NR

6. Seebacher et al. 2016 (1) and (2) ¹⁰⁹	Exp.	As above (larger trial of the Seebacher et al. 2015 study).	1 x Experienced physiotherapist (NR)	40 minutes (initial face-to-face group) 4 x 1 x NR (tel) 4 x 6 x 17 (motor imagery CD and practice)	Home-based and introductory group (NR) (group and individual: NA)	No	Yes	No
7. Sgoifo et al. 2017 ¹¹⁰	Exp.	NR: Based on Jacobson relaxation exercises	1 x Psychotherapist (NR)	8 x biweekly x 60 (face-to-face)	Hospital site	NR	Yes	Yes
8. Sutherland et al. 2005 ¹¹³	Exp.	NR: cites evidence for previously evaluated relaxation treatments only.	1 x Instructor (NR)	10 x 1 x NR (face-to-face)	Community and home-based (NR)	No	Yes (Homework only)	NR
9. van Kessel et al. 2008 ¹¹⁸	Ctrl.	NR: Relaxation techniques to control for therapist contact and support, expectations, homework tasks, and other non-specific treatment aspects.	1 x Clinical Psychologist (previously CBT trained)	Over 8 weeks 3 x 50 (face-to-face) Over 8 weeks 5 x 50 (tel)	Hospital facility (individual: Yes)	Yes	Yes	Yes
Combined Relaxation, Visualisation, Active imagination and Aerobic Exercise								
1. Zalisova et al. 2001 ¹³⁸	Exp.	Based on effects of different types of exercise in MS generally and Chronic Fatigue Syndrome	1 x Physiotherapist (not clear)	6 x 3 x 120 (face-to-face) Exercise: 6 x 5 x 60 (face-to-face)	Rehabilitation Centre (group and individual: NR)	NC	NR	NR
				Exercise intensity: 60% VO ₂ max				

Abbreviations: Ctrl (Control group); EC (Energy Conservation), Exp (Experimental group); MBCT (Mindfulness-based Cognitive therapy); MBSR (Mindfulness-based Stress Reduction); MI (Motivational interviewing); NR (Not reported); NA (not applicable); NC (Not clear from text). PA (Physical activity promotion); OT (Occupational therapist); PI (Principal investigator); PT (physiotherapist); SMART (Specific, Measurable, Activity-related, Realistic, and Time-specified or Time-limited goals and monitoring these etc); SPMS (Secondary progressive MS); Tel (telephone therapist support).

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